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Vol. IV MAY, 1919 No. 8

The Journal of Laboratory and Clinical Medicine

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The Journal of Laboratory and Clinical Medicine

VOL. IV. ST. LOUIS, MAY, 1919 No. 8

ORIGINAL ARTICLES

CLINICAL OBSERVATIONS CONCERNING THE FRAGILITY OF ERYTHROCYTES*

BY H. Z. GIFFIN, M.D., AND A. H. SANFORD, M.D., MAYO CLINIC, ROCHESTER, MINN.

ALTHOUGH many early studies concerning hemolysis had previously been made, Ribierre in his Paris thesis, published in 1903, was the first to clearly summarize the knowledge concerning corpuscular resistance and to devise a clinical method of practical value for the measurement of the resistance and fragility of erythrocytes. The methods formerly proposed required the use of more blood than could be obtained ordinarily for routine clinical work. Ribierre's method, however, is simple and with various modifications is in general use today. In his Paris thesis Ribierre discussed the existing knowledge concerning the various globulicidal agents and the mechanism of hemolysis, the different methods proposed for the measurement of resistance, and elaborated his own method. He studied especially and in detail, the increased resistance found in the different types of jaundice and endeavored to interpret the cause of this increased resistance.

It is a very curious fact that in Ribierre's exhaustive study of resistance in jaundice he should have overlooked the most important diagnostic discovery in connection with the subject. In other words, he failed to demonstrate the decreased resistance or rather increased fragility so constantly present in hemolytic jaundice.

*Presented before the American Society for Clinical Investigation, May 6, 1918, Atlantic City.

It remained for Chauffard, in 1907, to discover the fact that the erythrocytes in the peripheral circulation of patients with hemolytic jaundice, were abnormal, especially that they were more fragile. This finding has been corroborated in all later reports on the subject.

The use of hemolytic serums or of mechanical methods for testing the resistance of erythrocytes has not as yet proved of practical value and it is necessary to rely on an estimation of their resistance toward distilled water in hypisotonic salt solution.

Butler has published an exhaustive study on fragility of the red blood corpuscles. Daily examinations of his own blood over a period of months demonstrated that the degree of fragility was constant from day to day and that readings made at different times of the day were the same. His experiments showed that cells washed in salt solution were slightly more fragile, while cells washed in citrated saline were not affected by the procedure. Cells treated by oxygen were more resistant, while those treated by carbon dioxide were more fragile. He emphasized the fact that if comparable results are to be obtained by different workers, a constant dilution (1 to 10 by his method) of the blood must be used. Butler's readings for normal and his results on patients correspond in most instances with our own experience, although his method is different and our dilutions are approximately 1 to 25.

Hill obtained high readings as a result of the use of washed corpuscles. Davis concluded that he obtained less uniform results with washed corpuscles. Hill also demonstrated that the use of arsenic increased the resistance and that splenectomy lowered the point of complete hemolysis.

A word should be said concerning the importance in our own experience, of a control test in the estimation of fragility. The control test furnishes a method of determination of the accuracy of the salt solution used. Moreover with the use of a fixed normal, for example, of 0.34 per cent for maximal resistance, smaller variations in resistance can not be accurately interpreted. With the use of a control a variation of from 0.02 per cent to 0.04 per cent may be regarded as quite definite. In this way the use of a control test furnishes a better method of comparison and interpretation, in addition to its value as a test of the accuracy of the salt solution itself.

TECHNIC OF TEST FOR FRAGILITY OF ERYTHROCYTES

A review of the literature of diseases marked by blood destruction impresses one with the fact that there has been no uniformity in the various methods used in studying the fragility of the red blood cells.

The use of saponin need not be considered in connection with the present study. The work of M'Neil seems to indicate that a study of fragility with this hemolytic agent does not give results conforming in all respects to those obtained with hypisotonic salt solutions.

Most methods of testing the fragility of erythrocytes depend on the observation of the breaking up of the cells in salt solutions of various percentage strength, the chief difference lying in the method of making the various solutions, and of reading and reporting end-points, or degrees of hemolysis.

Karsner and Pearce employed Theobald Smith's method as modified by Gay. "Chemically pure sodium chloride was dried for two nours at 170° C. and immediately weighed in amounts necessary to make 500 c.c. volumes of salt solution ranging from 0.1 to 0.5 per cent in steps of 0.25 per cent. In order to be sure of approximately the same volume of corpuscles in the anemic as in the normal bloods, the gently defibrinated blood was centrifuged and the serum drawn off. One-tenth centimeter of the corpuscular mass was measured in a graduated pipette and placed in 3 c.c. of each of the various salt solutions. Standard colorimetric scales for comparison were made by laking red cells with distilled water; thus the laking of 0.4 c.c. of the corpuscular mass in 12 c.c. of distilled water represented a standard of 100 per cent hemolysis. Dilutions of this solution were made so as to have tubes showing the color values of 80, 60, 40, and 20 per cent hemolysis." Preliminary readings were made, and the mixtures placed in the incubator for eighteen hours when the results were finally read.

Butler describes his technic in detail. The essential difference in his method from others is in the manner of making his mixtures of blood and saline. He uses a Wright capillary pipette of fine bore with an arbitrary unit of measurement marked on the capillary portion of the tube. This small pipette is used for measuring nine units of saline solution of definite percentage strength into a miniature test tube made from ¼-inch glass tubing cut off in 1½-inch lengths and sealed at one end. This procedure is repeated using each one of the different stock saline solutions made fresh each day from a stock 1 per cent sodium chloride solution. Butler uses a burette for making dilutions of 1 per cent sodium chloride with distilled water in intervals of strength of 0.025 per cent. Generally the range employed is from 0.45 per cent to 0.30 per cent. In a few instances the strongest solution is 0.7 per cent. A single unit of blood drawn in the Wright pipette from a puncture of the thumb, is added to each of the small test tubes containing nine units of saline, so that his final mixture is always 1 to 10.

Hill has recently reported a method in which he used a definite amount of washed corpuscles (0.05 c.c.) in hypisotonic salt solutions of different percentages.

The method of Ribierre has seemed to us to be the most satisfactory simple method for accurately determining the fragility of erythrocytes. This author uses a stock solution of 0.5 per cent sodium chloride. In a series of small test tubes he places different amounts of this stock solution; in the first tube 50 drops, in the second 48, in the third 46, etc. To each tube is then added the number of drops of distilled water necessary to make the total volume of solution in each tube 50 drops. A definite amount of blood (20 cm.) measured with a graduated capillary pipette is added to each tube of solution. The various degrees of hemolysis from "slight" to "complete" are noted. Normally, hemolysis begins in the tube containing 44 drops of 0.5 per cent salt solution. The percentage of salt in this tube is 44/50 of 0.5 per cent, or 0.44 per cent. Our own modification of this method in detail is as follows:

The stock solution is made by dissolving 0.5 gm. sodium chloride (chemi-

Fig. 1.—Dilutions are made of 5 per cent sodium chloride solution by adding distilled water by the drop method, so that each tube contains twenty-five drops of hypisotonic solution.

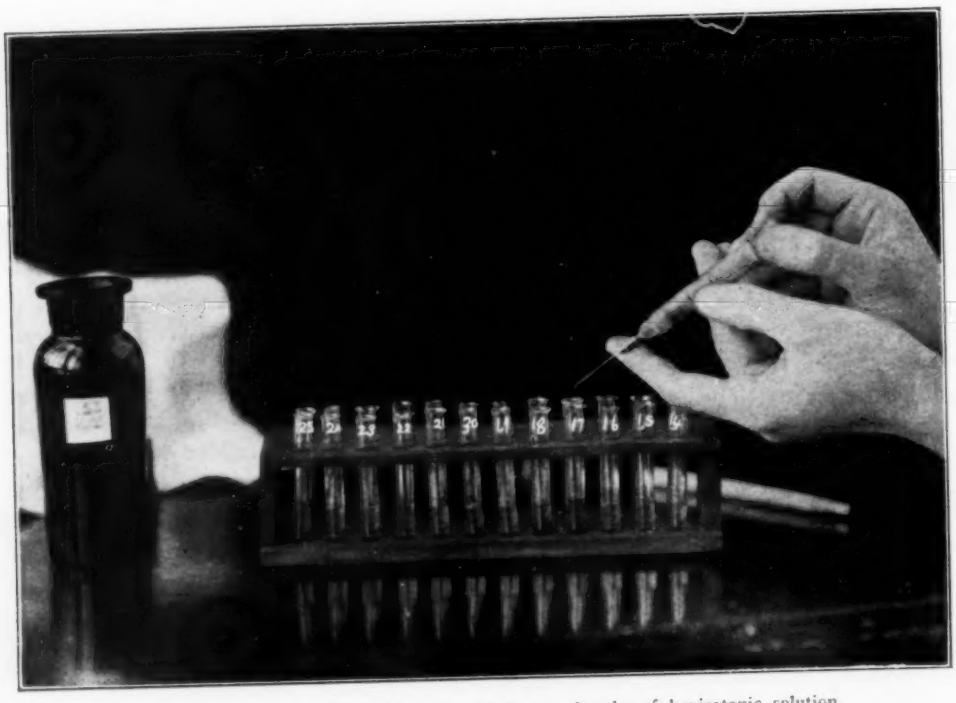

Fig. 2.—One drop of whole blood is added to each tube of hypisotonic solution.

cally pure and anhydrous) in 100 c.c. distilled water. Great care should be exercised in making this solution. A good balance must be used for weighing the salt, and a volumetric flask employed for measuring the water.

A twelve hole Wassermann rack, with at least two rows of holes, is filled with three-inch by three-eighths-inch tubes. The front row is for the patient's test, the back row for a control. The tubes in the front row are numbered with a glass marking-pencil, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, and 14. In each tube in the front row, and in the tube in the back row immediately behind it, is placed the number of drops of 0.5 per cent salt solution indicated by the figure marked on the tube in the front row. A capillary pipette drawn from soft glass tubing is used for putting the drops of salt solution in the tubes. With the same pipette distilled water is added drop by drop to each tube so that there is a total of 25 drops; for example a tube marked "20" should contain 20 drops of 0.5 per cent sodium chloride solution and 5 drops of distilled water, and the tube immediately behind it (control tube) should contain the same.

The patient is bled by puncturing the vein in the usual manner for obtaining blood for a Wassermann test. A rather small gauge needle should be used, and there should be no delay in getting the blood. An all glass syringe, sterilized by boiling, and thoroughly dried should be used. It is not necessary to rinse out with normal salt solution, in fact it would not be advisable as in this way an excess of salt might be added to the solutions in the tubes. One drop of blood should be allowed to fall into each tube of the front row. The tube should be thoroughly shaken to make an immediate corpuscle suspension. The plasma is greatly diluted and usually no fibrin is formed. If a slight clot forms it should be free from corpuscles.

In the back row (control tubes) should be placed blood obtained in a similar manner from a normal person. It may seem unnecessary to use a control in every test. In fact if several patients are being tested at one time, one control serves for all. The purpose of this test of normal blood is to insure that the salt solution is of the proper strength, as of course a very slight alteration makes a difference in the result. Every patient's blood, then, is considered not only in relation to the different strengths of salt solution determined by reckoning the dilutions in each tube, but also is compared with the behavior of supposedly normal corpuscles in solutions of exactly the same strength.

The tubes are allowed to stand an hour or two at room temperature and the results are then read. The dilution in which there is just a slight tingeing of the supernatant fluid due to the laking of a few of the least resistant corpuscles is noted as the point of initial hemolysis. Reading from left to right, the first tube in which it can be demonstrated that the hemoglobin is entirely free, and that there is no corpuscular residue evident by shaking the tube, indicates the point of complete hemolysis. The percentages of salt solution indicative of initial and complete hemolysis are readily reckoned; that is:

Tube marked 20 showing beginning hemolysis contains 20/25 of 0.5 per cent sodium chloride = 0.40 per cent sodium chloride.

Tube marked 16 showing complete hemolysis contains 16/25 of 0.5 per cent sodium chloride = 0.32 per cent sodium chloride.

The percentage can be immediately determined by multiplying the number on the tube by 0.02. Normal blood shows beginning hemolysis in 0.42 per cent to 0.38 per cent sodium chloride solutions and hemolysis to be complete in solutions of 0.36 per cent to 0.32 per cent sodium chloride. When initial and complete hemolysis occur in solutions stronger than normal an "increase of fragility" is present. When hemolysis occurs only in solutions weaker than those which lake normal blood, the cells under observation are more resistant than normal and such blood is reported as having an "increase of resistance."

It seems to us important to use chiefly the expressions "initial hemolysis," "complete hemolysis," "increase of fragility," and "increase of resistance" in order to obviate the confusion of terms which is apt to occur in a discussion of this subject.

CLINICAL RESULTS

We have had an opportunity to study a comparatively large group of cases of hemolytic jaundice, pernicious anemia, splenic anemia and myelocytic leucemia with respect to fragility, and the results, although largely of corroborative value, demonstrate certain interesting details.

TABLE I

FRAGILITY TESTS IN HEMOLYTIC JAUNDICE

Twenty-three Nonoperative and Preoperative Cases

CASE	*Percentage NaCl*				REMARKS
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT	
86218			.42	.46	
135948			.34	.40	
141268			.34	.40	
153245			.38	.46	
148209			.36	.40	Brother complete .42.
			.42	.44	
161538			.38	.44	
162670			.36	.40	
94675			.38	.44	
91298			.32	.40	
			.36	.40	
153653			.36	.42	Mother complete at .40. Nonoperative.
157525			.35	.38	Mother complete at .42. Nonoperative.
169405			.36	.42	No operation.
172287			.38	.42	Mild. No operation.
			.36	.42	
216019				.44	No operation.
205552			.36	.42	Father .46 — .40.
			.38	.40	
	.44	.46	.36	.38	
187817	.46	.50	.38	.46	No operation.
216591	.42	.46	.34	.38	
192817	.44	.50	.36	.42	
211816	.42	.48	.34	.40	
212273		.50		.40	Father .50 — .42.
190364		.46		.40	
190774		.50		.38	
	.44	.50	.34	.40	
212934	.46	.42	.36	.36	
Averages	.44	.478	.363	.412	

Hemolytic Jaundice, (25 Cases, Tables I, II, and III).—The fragility of erythrocytes has been estimated in twenty-five patients with hemolytic jaundice. These were all definite cases although some of them were mild. In twenty-three nonoperative and preoperative cases twenty-nine tests were made; in all but three there was a markedly increased fragility. In two of these three the point of complete hemolysis was 0.02 per cent higher than the controls. In one only of the entire group could the fragility be said to be normal; this was in a very mild but, from all standpoints, a definite case. It is an important fact that no case which from a clinical or surgical standpoint could be diagnosticated as primary hemolytic jaundice, showed an increase of resistance. The fact that hemolytic jaundice may occur with normal fragility is corroborated; but it is possible that observations at other times would show in the same patient an increased fragility. It is also probable that the increased fragility of hemolytic

TABLE II

FRAGILITY TESTS IN HEMOLYTIC JAUNDICE AFTER SPLENECTOMY (12 CASES)

CASE	*Percentage NaCl*				TIME AFTER SPLENECTOMY
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT	
112836			.34	.40	1 year 8 months.
			.36	.48	1 year 9 months.
141268			.36	.46	18 days.
142074			.38	.42	15 days.
153245			.34	.42	1 month.
148209			.36	.36	23 days.
			.36	.40	4 months.
	.42	.42	.36	.36	1 year 2 months.
161538			.34	.40	21 days.
162670			.32	.42	22 days.
			.36	.40	2 months.
	.42	.50	.32	.36	1 year 8 months.
94675			.32	.32	1 month.
216591	.44	.50	.32	.38	22 days.
190364	.46	.50	.36	.40	18 days.
192817	.38	.50	.32	.36	24 days.
212273	.46	.50	.34	.40	19 days.
Averages	.43	.486	.344	.396	

TABLE III

FRAGILITY TESTS—HEMOLYTIC JAUNDICE

	General Averages—Percentage NaCl			
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT
23 cases nonoperative and preoperative	.44	.478	.363	.412
12 cases postoperative (splenectomy)	.43	.486	.344	.396
10 cases preoperative	.43	.48	.363	.414
Same 10 cases postoperative	.43	.486	.34	.39

jaundice can be modified by long continued anemia and by a concurrent septic process even to the degree that an increase of resistance may be present.

The relatives of four patients with hemolytic jaundice were found to have an increased fragility, in two instances the father, in one the mother, and in another a brother. Two of these four relatives had no symptoms whatever of the disease, and in two of them the symptoms were first noted at the age of eighteen and twenty years. This would seem to indicate a definite hereditary factor even in cases in which an onset occurs in later life.

The averages in hemolytic jaundice for initial hemolysis were, controls 0.44 per cent, patients 0.478 per cent. The averages for complete hemolysis were controls 0.365 per cent, patients 0.413 per cent. The point of highest initial hemolysis was 0.50 per cent, the point of highest complete hemolysis was 0.46 per cent.

After splenectomy (Table II) for hemolytic jaundice seventeen tests were made in twelve cases. In general an increased fragility was present in estimations made fifteen days to one year and nine months after splenectomy. There was, however, a definite, although slight decrease of fragility with respect to complete hemolysis, although only two patients showed a normal resistance. One patient who had in all six tests, gave a return to normal for both initial and complete hemolysis one year and two months following operation. The point of initial hemolysis did not, however, show this definite shift toward normal after splenectomy.

The averages after splenectomy for hemolytic jaundice were for initial hemolysis controls, 0.43 per cent, patients 0.486 per cent. The averages for complete hemolysis were controls 0.344 per cent, patients 0.396 per cent.

In a total of 260 tests on 225 patients a definite increase in fragility, 0.04 per cent or more, was found in only four cases which were not hemolytic jaundice. This is no greater number than would be accounted for by errors of technic. These cases were, respectively, an acute lymphatic leucemia, a lymphosarcoma, an inoperable carcinoma of the stomach, and an indefinite case with splenomegaly and arthritis. Increased fragility in cases with cyanosis has been noted by others in a few instances. By these observations the value of the fragility test in the diagnosis of hemolytic jaundice is conversely demonstrated; that is the finding of a definite increase of fragility is almost certain evidence of the existence of hemolytic jaundice.

Butler has shown that both washed (sodium chloride) and unwashed corpuscles of patients with hemolytic jaundice show an increased fragility; and that, as with normal cells, oxygen increases their resistance slightly while carbon dioxide increases their fragility. He reports six cases occurring in two families. Davis corroborates the findings with respect to washed corpuscles.

Myelocytic and Lymphocytic Leucemia.—The resistance of the erythrocytes is shown to be normal in myelocytic leucemia (12 cases, Table IV). There may be a slight general tendency toward an increase of resistance, but this is not of a definite nature. The averages were, for initial hemolysis, controls 0.42, patients 0.436, for complete hemolysis controls 0.348, patients 0.333. Patients were tested before and after the application of radium over the spleen and it

was thought in two instances that an increased fragility followed the use of radium. This observation did not, however, prove to be constant. Three cases

TABLE IV

FRAGILITY TEST—MYELOCYTIC LEUCEMIA (12 CASES)

CASE	MINIMUM RESISTANCE CONTROL	MINIMUM RESISTANCE PATIENT	MAXIMUM RESISTANCE CONTROL	MAXIMUM RESISTANCE PATIENT	DATE
173747	....	....	.36	.36	10- 2-16
180499	....	.46	....	.38	5- 9-17
173740	....	....	.36	.36	10- 2-16
221207	....	.46	....	.34	2-12-18
194399	.44	.42	.36	.34	5-16-17
221664	.40	.46	.32	.36	2-11-18
	.42	.46	.36	.34	2-15-18
173772	....	....	....	.34	9-29-16
194933	.42	.42	.34	.30	5-28-17
207035	.46	.46	.38	.32	9- 6-17
220165	.46	.40	.34	.30	2-12-18
	.42	.44	.36	.34	1-28-18
168742	....	....	.34	.34	8-22-16
	....	....	.36	.28	2- 2-17
192150	.34	.38	.30	.30	4-28-17
Averages	.42	.436	.348	.333	

of lymphocytic leucemia were tested, two of them showed normal resistance and one, an acute case, a slight increase of fragility. Butler noted normal fragility in two cases of myelemia and one of lymphemia.

Splenic Anemia (14 Cases, Table V).—The cases of splenic anemia in this group were carefully selected. Identifiable cases of chronic septic splenomegaly, luetic splenomegaly, cirrhosis of the liver and, so far as possible, all of those diseases which have been so commonly confused with splenic anemia in the literature were excluded. In most of the cases of splenic anemia a definite increased resistance was shown. The averages for the fourteen cases were, for initial hemolysis controls 0.438, patients 0.402. Complete hemolysis controls 0.353, patients 0.316, with an average hemoglobin of 44 per cent. There seemed to be still more definite increase of resistance following splenectomy.

Karsner and Pearce have demonstrated an increase of resistance experimentally following splenectomy in animals; it occurred in association with the anemia, apparently due to splenectomy. The increased resistance following splenectomy for splenic anemia in man occurs without apparent relationship to the already existent anemia. One patient showed complete hemolysis, less than 0.28 per cent, two years and ten months after operation. The increased resistance in cases of splenic anemia preceding splenectomy may be entirely secondary to the chronic anemia. There is, however, a similarity to the increased resistance of cases of portal cirrhosis in which anemia of a definite degree has never been present. Hill found normal fragility in two cases of splenic anemia.

Pernicious Anemia (18 Cases, Table VI).—Although pernicious anemia has certain features that are similar to hemolytic jaundice, there is no similarity in

the behavior of the erythrocytes to hypisotonic salt solution. The resistance of the red cells is usually definitely increased in pernicious anemia although in some of the cases it is normal. The averages for eighteen cases were, for initial

TABLE V

FRAGILITY TEST IN SPLENIC ANEMIA (14 CASES)

CASE	*Percentage NaCl*				Hb.	R. B. C. IN MILLIONS
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT		
224466	.40	.44	.34	.36	52	3.16
161083			.36	.36	50	4.54
165779			.34	.34	34	3.46
158085			.36	.36	45	3.33
214034	.44	.38	.38	.30	52	3.28
		.38		.28		
167319			.30	.30	73	4.91
216004		.42		.32	38	2.57
214146	.42	.40	.34	.30	26	2.38
144914	.42	.42	.34	.34	63	3.52
215670	.46	.42	.36	.34	15	1.57
191277	.44	.44	.36	.30	62	3.96
	.42	.40	.34	.28 —	45	3.77
209234	.48	.42	.38	.32	20	2.54
119565	.44	.30	.38	.28 —	30	2.08
129358	.46	.40	.36	.28	60	4.3
Averages	.438	.402	.353	.316	44.3	3.28

TABLE VI

FRAGILITY TEST IN PERNICIOUS ANEMIA (18 CASES)

CASE	*Percentage NaCl*				Hb.	R. B. C. IN MILLIONS	TIME AFTER SPLENECTOMY
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT			
188649	.44	.40	.36	.32	55	2.49	
212480	.44	.38	.38	.34	33	1.33	
139695			.36	.28	30	1.78	7 months.
158136			.36	.30	28	1.51	7 weeks.
162242			.34	.24	50	1.9	
220132	.42	.40	.36	.32	43	1.67	
151088			.36	.30	41	1.98	4 months.
153395			.32	.30	75	3.81	3 months.
157290			.32	.30	84	5.2	18 days.
188717			.38	.36	30	1.31	
197254	.42	.42	.36	.36	40	1.51	
181414			.36	.36	19	1.03	
160970			.38	.32	50	2.57	
170115			.36	.36	39	2.44	
129968				.32	71	2.6	3 weeks.
164775			.34	.34	29	1.9	
196267	.42	.44	.32	.34	33	1.74	
124257			.38	.34	68	4.28	3 months
Averages	.428	.408	.355	.322	45.4	2.28	

hemolysis, controls 0.428, patients 0.408, complete hemolysis controls 0.355, patients 0.322, with the hemoglobin averaging 45 per cent and the red cell count 2,280,000. It is possible that the increase of resistance has been due to the chronic anemia present.

Again, as with splenic anemia, the resistance of erythrocytes is increased quite definitely after splenectomy. This fact I believe has not been previously shown so clearly in any other series of cases.

Hill, using washed corpuscles, found that fragility in thirteen cases of per-

TABLE VII

FRAGILITY TESTS IN PURPURA (4 CASES)

CASE	*Percentage NaCl*			
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT
12155	.46	.46	.34	.34
212138	.46	.44	.36	.36
214778	.42	.42	.34	.34
228359	.40	.40	.32	.32
Averages	.435	.43	.34	.34

TABLE VIII

FRAGILITY IN ANEMIA OF SECONDARY TYPE (11 Cases)

CASE	*Percentage NaCl*				Hb.	R. B. C. IN MILLIONS	REMARKS
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT			
212144		.42		.34	45	3.99	Colitis.
156102			.34	.28	29	3.68	Ulcer.
221504	.44	.40	.36	.28	30	3.71	Ovarian cyst.
179009			.38	.30	28	2.6	Cellulitis.
166483			.32	.32	39	3.52	Myomas.
162653			.34	.24	29	2.38	Hemorrhoids.
210376	.46	.46	.38	.30	42	4.0	Hemorrhoids.
195342	.42	.42	.32	.28	35	3.04	Colitis.
159417			.34	.34	38	3.99	Myomas.
208004	.44	.44	.36	.34	37	3.56	Hematuria.
221439	.38	.40	.34	.32	48	2.97	Sepsis.
Averages	.425	.424	.349	.308	38.3	3.503	

nicious anemia was either high, low or normal, while Davis' findings more nearly agree with ours in that they demonstrate usually an increased resistance.

Purpura (4 Cases, Table VII).—Fragility tests in four patients with severe forms of purpura demonstrate normal values. There is no variation whatever from normal and although the series is small, the results are sufficiently definite to be indicative. Butler obtained normal readings in one case of purpura.

Severe Anemia of Secondary Type (11 Cases, Table VIII.)—Anemia of low color index, whether due to hemorrhage or a chronic infectious process, is

most apt to be associated with an increased resistance of the erythrocytes. Normal resistance is seen in some instances, but the averages show a fall of 0.04 per cent for complete hemolysis. The degree of anemia bears a relationship in most of the cases to the increase of resistance. The readings are quite comparable to those of pernicious anemia. Similar conclusions were drawn by Hill.

Chronic Obstructive Jaundice (12 Cases, Table IX).—The averages obtained in cases with chronic jaundice of the obstructive type are, for initial hemolysis 0.396 per cent and for complete hemolysis 0.31 per cent. A definite increase in resistance is demonstrated. Certain cases of chronic obstructive

TABLE IX

FRAGILITY TEST IN CHRONIC OBSTRUCTIVE JAUNDICE (12 CASES)

CASE	*Percentage NaCl*				REMARKS
	INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT	
206433	.40	.40	.32	.32	No operation; probable cancer, gall bladder and chronic jaundice (3).
157154			.30	.30	Stone common duct, jaundice (3) 3 months.
167420			.32	.32	Biliary cirrhosis, splenectomy, jaundice (3).
189394	.46	.42	.36	.32	Stones, G. B., pancreatitis, cirrhosis, jaundice (2).
156252			.36	.28	Cirrhosis of liver, ascites, jaundice (2), 1 year.
170914			.36	.28	Chr. pancreatitis common duct, obstructive jaundice (3), 6 weeks.
217651	.42	.36	.36	.18	Carcinoma (?), pancreas, jaundice (2), 1 month.
223891	.42	.38	.32	.28	Sandy muddy material common duct, jaundice (2).
180780			.32	.28	Subacute pancreatitis, cancer (?), Hypertrophic cirrhosis.
192980	.44	.42	.36	.28	Stones in gall bladder, suppurative cholangitis, pruritis.
210429	.48	.40	.38	.28	Traum. strict. common duct, complete closure, jaundice.
201168				.28—	No operation, jaundice (2), 1 year, gall bladder, enlarged liver.
Averages	.436	.396	.342	.31	

jaundice give approximately normal readings, but in the large majority of instances resistance is markedly increased. Whether this is due entirely to the jaundice or also to factors present as a result of complications, can not be determined. There is some reason to conclude that chronic septic and toxic processes, as well as bile pigments, increase the resistance of erythrocytes, and it is probable that cirrhosis of the liver, pancreatitis and gall bladder and duct infections, as well as the jaundice itself, may be factors affecting corpuscular resistance. Ribierre's thesis contains a most interesting study of the factors affecting fragility in obstructive jaundice. Subsequent observers have corroborated his clinical findings.

We have not reported in this paper the results on a large number of

miscellaneous cases. Conclusions may be drawn only when a group of cases has been studied; isolated findings may be misleading (Table X).

SUMMARY

A total of 260 tests in 225 cases is the basis for this report. A modified and somewhat simplified Ribierre method has been used.

1. Twenty-five patients with hemolytic jaundice were examined. In all but three there was a markedly increased fragility. Two of these three showed an increased fragility of 0.02 per cent. In only one could the resistance be said to be normal. Of the entire group of 225 cases there were only four with definitely increased fragility in which a diagnosis of hemolytic jaundice could not be made. Relatives of four patients with hemolytic jaundice were found to have an increased fragility; two of these four relatives had no symptoms of the disease, and in the patients themselves the onset of the disease dated to the age of eighteen or twenty years, indicating a hereditary factor even though the onset was late. After splenectomy there was found a slight decrease in the degree of fragility, especially with respect to initial hemolysis.

2. Twelve cases of myelocytic leucemia showed normal fragility with very slight variations toward increased resistance.

3. In fourteen cases of splenic anemia, excluding so far as possible all those conditions so commonly confused with splenic anemia, a definitely increased resistance of erythrocytes was shown. A still greater increase of resistance was demonstrated after splenectomy.

4. In pernicious anemia (18 cases) the resistance of erythrocytes was slightly increased. Here again after splenectomy there was a more definite increase of resistance.

5. Four cases of severe purpura showed a strikingly normal hemolysis without variations.

TABLE X

FRAGILITY OF ERYTHROCYTES

	NUMBER CASES	*Percentage NaCl*			
		AVERAGES		AVERAGES	
		INITIAL CONTROL	HEMOLYSIS PATIENT	COMPLETE CONTROL	HEMOLYSIS PATIENT
Hemolytic jaundice (non-operative and preoperative)	23	.44	.478	.363	.412
Hemolytic jaundice (after splenectomy)	12	.43	.486	.344	.396
Myelocytic leucemia	12	.42	.436	.348	.333
Splenic anemia	14	.438	.402	.353	.316
Pernicious anemia	18	.428	.408	.355	.322
Purpura	4	.435	.43	.34	.34
Secondary anemia	11	.425	.424	.349	.308
Chronic obstructive jaundice	12	.436	.396	.342	.31

6. Anemia of low color index, whether due to hemorrhage or to chronic sepsis, was accompanied by an increase of resistance.

7. In eleven cases of chronic obstructive jaundice in general an increase of resistance was shown.

The test for fragility of erythrocytes in hypisotonic salt solution is of definite practical value especially in the diagnosis of all those diseases which may simulate hemolytic jaundice. It is more accurate when compared with a control test of normal blood.

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SOME STUDIES IN PLASMOGENESIS*

By Alphonso L. Herrera, Mexico City, Mexico.†

I HAVE proposed the name "Plasmogenesis" to cover that group of studies which has existed since the time of Dutrochet's first investigations dealing with the origin of protoplasm. For more than twenty years past I have done work in this field, which with that of Traube, Leduc, Bütschli, Quincke, Harting, Slack, Fischer, and others, now makes up a voluminous literature.[1] The science covers not only the attempts which have been made to reproduce the forms of cells and of lower organisms, but all those at the synthesis of albumins, ferments, lipoids, etc.

My personal endeavors have been directed to the problem of producing artificial cells intended to mimic as perfectly as possible the structures of nature. My first experiments were made with organic substances like tannin, oleic acid,

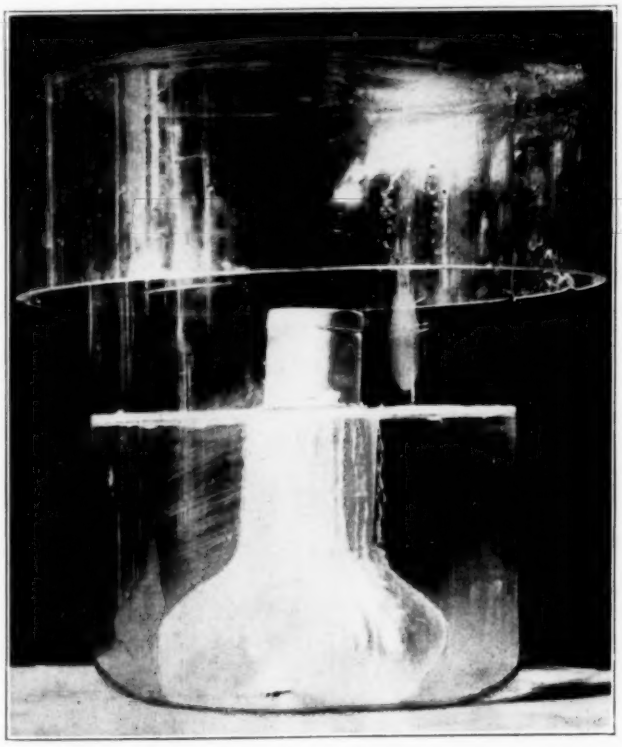

Fig. 1

Fig. 2

albumin and fats. I soon noticed, however, that some of my best results were dependent upon the presence of mineral impurities in the substances employed, more particularly soluble silicates, which with certain salts like calcium chloride

*Translated from the Spanish by Daric Gutiérrez-Laserna of Bogata, Colombia, S. A.

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produce precipitation membranes. During the past years, I have bestowed intensive study upon the artificial forms shown by such silicate precipitates.[2]

Careful investigation has shown me that colloid silicic acid and the colloid silicates yield structures most like natural forms when produced from reaction

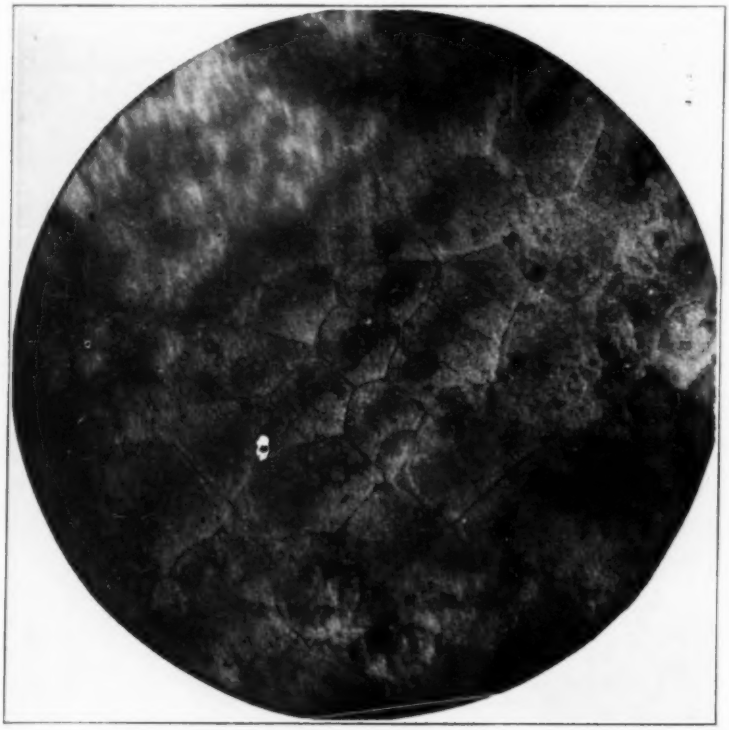

Fig. 3

Fig. 4

Fig. 5

mixtures of very low concentration, when contact between the precipitating agents is slow and when viscosity of the reacting solutions is great.

In 1917 I observed that the employment of double salts capable of entering into double decomposition with a second salt, yielded mixtures of crystalloid and colloid which mimic in wonderful fashion cells and other organized forms such

as amebæ. To produce these structures I began with a saturated solution of potassium silicate which had been saturated with potassium carbonate. A drop of this was placed on a slide and this covered with a second of calcium chloride. When the solution of potassium silico-carbonate had a sufficient concentration (a specific gravity over 1580), crystals of potassium chloride began to separate out, which little by little lost their sharp outlines and changed into osmotic balls

Fig. 6

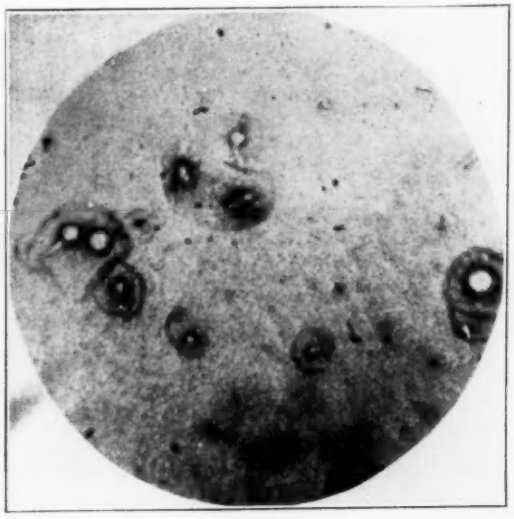

Fig. 7

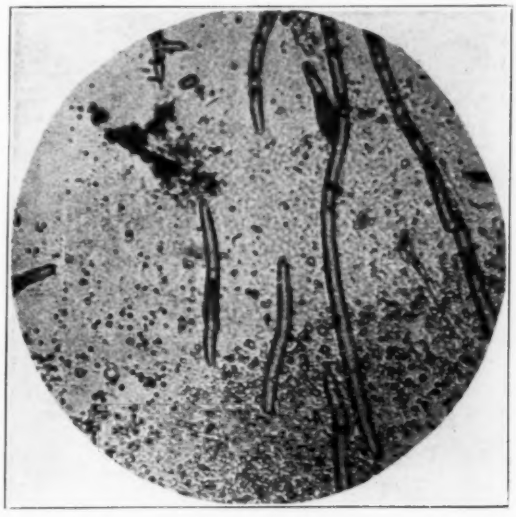

Fig. 8

looking like cells and amebæ which moved about slowly. These structures could be washed, stained and preserved in Canada balsam.[3]

In 1918 I observed that better results were obtained when the two solutions were allowed to diffuse into each other through a thin porous wall. If a Chamberland filter or an ordinary unglazed porous cup is filled with a solution of

potassium silico-carbonate and this is then immersed in a beaker containing one per cent calcium chloride (Fig. 1) there appear, by the next day, upon the surface of the porous cup, numerous tubules which, when observed microscopically, are seen to consist of beautiful hexagonal cells (Fig. 2) often showing nuclei (Figs. 3, 4, and 5) and sometimes figures resembling karyokinesis (Fig. 6).

Fig. 9

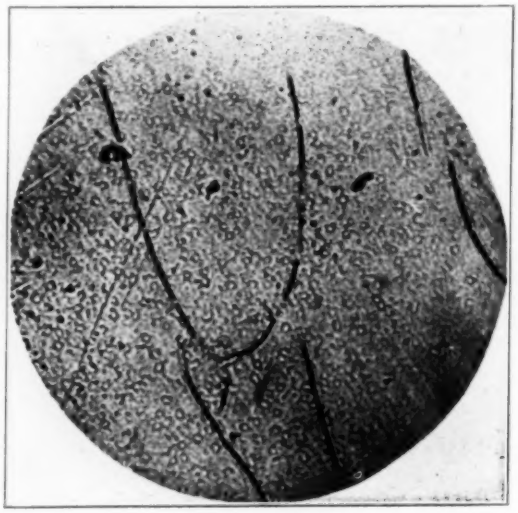

Fig. 10

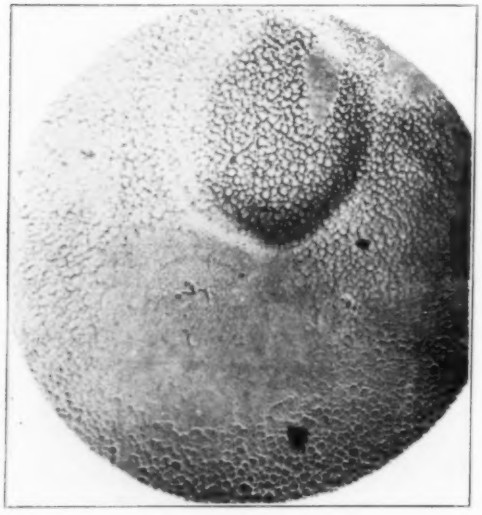

Fig. 11

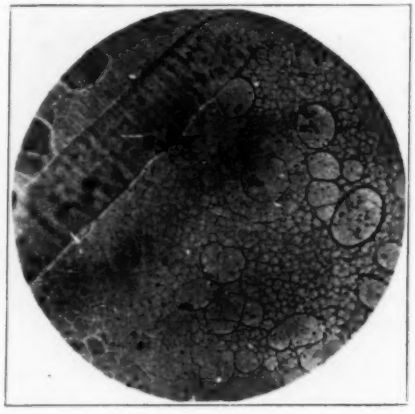

Fig. 12

I have sent many such preparations to my colleagues abroad for their personal study. Cells thus produced resemble very closely those of nature.

Cellular structures thus produced are easily destroyed by acids. To avoid this I have made silicate figures by employing another double salt, namely, that of the silico-fluorides. For this purpose I merely expose an ordinary glass slide to the vapors emanating from a bottle filled with hydrofluoric acid.

After the vapors have acted upon the glass for two or three days the slide is washed and stained with Kühne's blue. The microscope reveals numerous structures looking like isolated cells (Fig. 7), lower organisms (Fig. 8), spores and streptococcal chains (Fig. 9), bacteria (Fig. 10), and the micellar structures of protoplasm (Figs. 11 and 12), all produced in consequence of the formation of insoluble colloid silico-fluorides, and more or less hardened by an excess of hydrofluoric acid. The best structures are produced at a distance from the point where the vapors attack the glass most intensely.

I hold that these studies on the structures exhibited by colloid silicates are not without biological significance. Quite apart from the fact that the production of such structures and their identity with the morphology of living protoplasm indicates that the *physical* basis underlying the two must have much in common. I believe also that a parallelism exists from a *chemical* point of view. Has living protoplasm also an inorganic skeleton upon which is superimposed a "body and flesh" of such organic materials as the albumins? I incline to a positive answer in this matter because, on the one hand, the silicon compounds are widely distributed throughout the living world (a point to which I have repeatedly called attention in years past), while, on the other, the opinion that living matter consists exclusively of albumins can hardly be said to have been proved. The albumin theory may be true, but it is a significant fact that artificial cells mimicking in their morphology the living have not thus far been produced from albumin. They may, of course, be produced in the future in which case support will be given to Pflüger's theory regarding the origin of life on this planet by way of the cyanogen compounds; but until such proofs are forthcoming, a study of such inorganic cells as I have described is to be recommended.

Of the two theories, that which holds that life may have had its beginnings in inorganic materials is the easier, for albumins, fats, formalin, glycolic acid, etc., are all labile substances and hardly conceivable as existent in a primitive world. On the other hand, the interaction of solutions produced by the action of water and of atmosphere upon the earthy constituents of the soil is able to produce at once all the cellular structures which I have described.

I do not pretend to have proved through my experiments that such has been the source of living things upon this earth, but I do believe that I have at least obtained some evidence in this direction.

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TYPES OF PNEUMOCOCCUS IN LOBAR PNEUMONIA*

By Russell Richardson, M.D., Philadelphia, Pa.

PNEUMONIA has, in recent years, become one of the greatest scourges of the civilized world. There are few regions where it is not found. Especially is it prevalent where many people are moved from their native surroundings to a climate which is different from that to which they are accustomed. The reports of our health departments show such an increase that, at present, when tuberculosis is decreasing, pneumonia during several months of the year holds first place as a cause of death. Notwithstanding the importance of the disease and the large amount of work that has been done upon it we have made little if any decrease in its mortality. Our very treatment shows our helplessness in the face of the disease. We can only stand by to support the patient with our treatment while he fights his own battle. This he does by means of antibodies as we now know. However if he lacks the ability to form these in sufficient amount our supporting treatment is useless. Since the latter part of the last century attempts have been made to supply these antibodies in sufficient concentration to terminate the infection. Eyre and Washburn[1] tried for protective bodies a serum made by Dr. Pane of Naples. They used three cultures of pneumococcus from cases of pneumonia, one from a case of empyema following pneumonia, and one from the mouth of a normal individual. The serum protected in high dilution against two of the pneumonia cultures and the empyema culture, very slightly against the normal culture and not at all against the third pneumonia culture.

Neufeld[2] demonstrated as a probable explanation of such results as the above, that there were varieties of pneumococci which, though resembling each other morphologically, nevertheless showed very distinct immunologic differences. Dochez and Gillespie[3] followed this with a more detailed study dividing the strains of pneumococci into four types or groups. These they numbered I, II, III, and IV. Groups I and II were identical with the two organisms with which Neufeld had worked. They differed from each other only slightly morphologically but immunologically they were entirely distinct. These immunologic differences they demonstrated by animal protection and agglutination. Group III was the organism otherwise known as pneumococcus mucosus. It is unlike the other groups morphologically, as well as in its immune properties. Group IV was a heterogeneous group comprising all those cultures which did not belong in one of the other groups. These organisms somewhat resembled Groups I and II morphologically but did not interact immunologically either

Table I

TYPE	NUMBER OF CASES	PER CENT
I	28	45
II	12	20
III	9	14
IV	13	22

*From the Ayer Laboratory of the Pennsylvania Hospital.

with the other groups or among themselves. This classification has been the standard followed by all later work. The first 62 cases of pneumonia studied they found distributed as shown in Table I.

A continuation of this work for the following years at the Hospital of the Rockefeller Institute gave results closely approximating Table I.[4] The result of four years' examination of cases there is shown in Table II.[5]

TABLE II

TYPES	1912-13	1913-14	1914-15	1915-16	TOTAL	PER CENT
I	29	22	21	33	105	33.54
II	8	28	35	28	99	31.62
III	7	6	9	13	35	11.18
IV	16	13	17	28	74	23.64

The mortality of the different types varies greatly as shown by Cole.[6] Type III is by far the most fatal, Type II being generally considerably less so, and Type I slightly less fatal than Type II. Type IV is not nearly so severe an infection and has a correspondingly low mortality. The mortality of 103 cases as given by Cole is shown in Table III.

TABLE III

TYPE	NUMBER OF CASES	DEATHS	PER CENT
I	28	7	25
II	25	9	36
III	17	8	47
IV	33	2	6

Lister[7] working on pneumonia in South Africa has found five groups of pneumococci. Three of these groups are identical with Groups I, II, and III as found in this country, while two others, which are prevalent among the natives there, have not been found here.[8]

Mathers[9] in Chicago during the winter of 1914-15 found the distribution of types remarkably like the results at the Rockefeller Institute except that the predominating type differed. In New York Type II was found in the greater number of cases and in Chicago Type I. Table IV shows the results of this work.

TABLE IV

TYPE	NUMBER OF CASES	PER CENT	DEATHS	PER CENT
I	50	45.	13	26
II	25	22.5	7	28
III	5	4.5	4	80
IV	31	28	8	25

The mortality among these cases also bears a striking resemblance to the others. So few cases of Type III are found that the percentage of mortality varies more than the other types.

Clough[10] at the Johns Hopkins Hospital had very few Type II cases as com-

pared with other workers, and no deaths, while Type IV showed the high mortality of 57.2 per cent. The distribution of types among 54 cases is shown in Table V.

TABLE V

TYPE	NUMBER OF CASES	PER CENT	DEATHS	PER CENT	COMPLICATIONS	PER CENT	LEUCOCYTOSIS
I	19	35.2	7	36.8	6	31.6	24,100
II	3	5.5	0	0	1	33.3	27,300
III	8	14.8	8	100	4	50	11,800
IV	14	25.9	8	57.2	5	35.7	24,600
Atyp. II	9	16.7	4	44.4	2	22.	22,800

It will be noticed also that the Type III cases had the remarkable mortality of 100 per cent. These cases always have a high mortality, but seldom as high as in this series.

Frissell and Famulener[11] in New York found among 19 cases no Type III, and a rather large number of Type I cases. Their results are shown in Table VI.

TABLE VI

TYPE	NUMBER OF CASES	PER CENT	
I	9	50	1 death
II	7	38.8	4 "
III	0	0	
IV	2	11.1	1 "

In Pittsburg at the Allegheny General Hospital Hartman and Lacy,[12] examining 99 cases, found the distribution and mortality closely agreeing with earlier results. Their figures are shown in Table VII.

TABLE VII

TYPE	NUMBER OF CASES	PER CENT	DEATHS	PER CENT
I	41	41.4	15	36.5
II	29	29.3	10	34.5
III	6	6	4	66.6
IV	23	23.2	6	26

Notwithstanding the difficulty of obtaining satisfactory specimens for examination from children, a considerable number of these cases have been investigated.[13, 14, 15, 16] The results of these examinations point to an increased percentage of Type IV cases with a higher mortality in this type.

During the stay of the troops on the Mexican border Nichols,[17] investigating the pneumonia epidemic there, found a high percentage of typical types, especially Types I and II. Some of his cases were treated, probably thus accounting for the low mortality in Type I. His results are given in Table VIII.

TABLE VIII

TYPE	NUMBER OF CASES	PER CENT	MORTALITY, PER CENT
I	84	56	14.8
II	33	22	30.0
III	3	2	33.0
IV	30	20	13.3

During the past year type determinations have been carried on at the various army cantonments. McClelland[18] at Camp Beauregard found the distribution and mortality as follows:

TABLE IX

TYPE	NUMBER OF CASES	PER CENT	MORTALITY NUMBER OF CASES	MORTALITY PER CENT
I	33	29.2	4 (serum used)	12.1
II	11	9.7	1	9.1
III	5	4.4	1	20.0
IV	64	56.7	6	9.4

The work at Camp Funston, Kansas, gave results in 135 cases similar to those of McClelland except that the Type II cases made up a slightly larger percentage of the total.[19] Dick[20] at Camp Pike found that 48 per cent of 60 cases examined showed pneumococci, and of these there were 21 per cent Type I, 34 per cent Type II, and 45 per cent Type IV. Only one case of Type III was observed.

In the present work type determinations were made in 413 cases of lobar pneumonia during the winters from 1913 to 1917. Only cases between October 1 and May 1 are included. During the second, third and fourth winters serum was used in the treatment of Type I and part of Type II cases, after the method used by Cole at the Rockefeller Hospital, and so the mortality for these two types is given for only the first year.

The determinations were made on the basis of agglutination together with cultural and morphologic characteristics. A 24-hour broth culture was used with an equal amount of immune serum, obtained from the Hospital of the Rockefeller Institute. At first the serum was used undiluted but later in dilutions of 1:10. This was done with both Type I and Type II sera, controls being used in each case. If the strain in question did not agglutinate with either serum, the differentiation between Groups III and IV was then made on the basis of morphology and growth, which are very distinctive. When a rapid differentiation was wanted the following method was used: There was injected into the peritoneal cavity of one or two white mice from one-half to one c.c. of sputum rubbed up with normal saline solution. After two to four hours, if a peritoneal puncture showed many organisms, the mouse was killed and an agglutination test made, using a suspension of the peritoneal fluid. Some of the fluid was inoculated into broth and incubated for two hours and another agglutination test made on this culture. A precipitin test was also done in most cases. At the same time a culture was made from the heart blood and an agglutination reaction done later on this to control the first reaction. Especial care was taken to rule out any strains of streptococci which are the organisms in so many cases of pneumonia.

During the season of 1913-14, determination of types was made on 115 cases. These were distributed among the types as shown in Table X. The mortality is also shown.

TABLE X

TYPE	NUMBER OF CASES	PER CENT	DEATHS	PER CENT
I	39	33.9	12	30
II	28	24.3	7	25
III	6	5.2	3	50
IV	40	34.7	5	12

During the winters of 1914 to 1917 there were 308 examinations made. These are given in Table XI.

TABLE XI

TYPE	1914-15		1915-16		1916-17	
I	27	31.3%	17	20.7%	34	26.3%
II	12	13.9%	21	25.6%	26	20.1%
III	7	8.1%	10	12.0%	11	8.5%
IV	40	46.5%	33	41.4%	58	44.9%
Totals	86		81		129	

The normal mortality of Groups I and II it is not possible to estimate, because of the use of serum in these cases. The mortality of Groups III and IV was as follows:

TABLE XII

TYPE	1914-15		1915-16		1916-17	
III	3	43%	4	40 %	5	45.4%
IV	8	20%	6	17.6%	13	19.1%

Five cases presented a combination of two types. Two cases had Types I and III, both of which died. Two cases had Types II and III combined and one had Types I and IV. All of these recovered. It will be noticed in comparing these tables that, both in distribution and mortality, there is more or less agreement, within limits, between epidemics of different years. The scattering pneumonias of the summer season, which have not been included in this series, are generally in our experience Type IV cases.

In order to find out what differences there might be in the infections caused by organisms of these groups, a study was made of the typical symptoms of the disease and some of its complications. The symptoms chosen were cough, pain in chest, dyspnea and chill. These with the leucocytosis make up so large a part of the early picture of pneumonia. Table XIII shows the percentage of cases of each type in which these symptoms were present.

TABLE XIII

TYPE	COUGH	PAIN	DYSPNEA		CHILL
I	88%	81%	74%	severe 46% mild 28%	73%
II	90%	87%	70%		67%
III	75%	75%	75%		62%
IV	81%	91%	57%	severe 15% mild 42%	87%

As will be seen, the percentage of cases showing cough and pain does not vary noticeably in the four groups. On the other hand, with regard to dyspnea and chill, there is a considerable difference. The so-called typical groups, i. e., I, II, and III, show a higher percentage of dyspnea and a lower percentage of chill than do the heterogeneous. The term "chill" was not used in regard to chilly sensations, but only to a distinct shaking chill. The number of cases of type III are so few that it is not possible to place much importance on the figures for that group.

The average leucocytosis, on the other hand, shows a marked similarity in all four groups:

TABLE XIV

TYPE	LEUCOCYTES
I	20,900
II	16,700
III	21,800
IV	18,000

Of the complications of pneumonia there were studied meningitis, pulmonary tuberculosis, delayed resolution, lung abscess, empyema and endocarditis. In Table XIV are shown the number of cases of each which occurred in the various groups. Only cases of the first year, when serum was not used, are given.

TABLE XV

TYPE	MENINGITIS	PULMON. TUB.	DELAYED RESOLUTION	LUNG ABSCESS	EMPYEMA	ENDOCARDITIS	TOTAL
I	–	4	–	1	1	1	7
II	–	–	–	2	–	–	2
III	1	1	–	–	–	–	2
IV	1	2	3	–	6	1	13

Perhaps the most interesting point in regard to the distribution of the complications is that about twice as many were found in the Type IV cases as in any other group. One case of pneumococcus meningitis caused by a Type I organism came to the hospital. A history of preceding pneumonia was not obtained. The tuberculosis became evident on the clearing up of the pneumonia, though in how many cases it had been there before it is not possible to say.

On questioning the patients regarding what they considered to be the cause of their pneumonia, it was found that a large number of those with Type IV infection were able to remember a distinct occurrence to which they attributed their illness. Such exposures as sitting in a draft when warm, an engineer coming out from the hot engine room on a cold night, a man going outdoors after being in a warm swimming tank, etc., were a common history. Type IV organisms are commonly present in the mouth forming a constant source of infection in cases such as these. Lyall,[21] examining tuberculosis patients, found that when pneumococci were present in the mouth very few were other than Type IV. Studies in this laboratory on normal individuals and on those with slight coryza show-

that Type IV is apparently predominant in number. Dochez and Avery[22] have shown that the typical types usually disappear from the mouths of convalescent pneumonia patients in from 12 to 90 days, leaving only Type IV, if any, present.

On the other hand, those patients with infection of the typical types became ill without any apparent cause. The onset was that of a true epidemic infection, without any noticeable loss of resistance preceding. Nichols,[23] working on pneumonia in the army, where on account of age and physical condition, diminished resistance should not be a large factor, found 78 per cent of cases caused by typical types. It would seem then that the infections caused by the typical and atypical types may differ more or less. The latter, being less virulent, may need in most cases a loss of individual resistance for its development, while the former are more truly an epidemic infection, though the lessening of resistance may be a factor in these cases also. The greater number of complications in cases infected with a less virulent organism also lead toward this conclusion.

The unfailing regularity with which the same type of organism is found in several specimens of sputum from the same case of pneumonia, and the specificity of the agglutinations are of great importance in the practical application of this work to the serum treatment of pneumonia. The number of cases in which the type has been determined, widespread as they are, show that at least one-fourth of all cases are Type I which is now amenable to serum treatment, and that from one-half to three-fourths are caused by the typical types for which we may hope to have a satisfactory serum later.

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LABORATORY METHODS

A SIMPLE METHOD FOR THE PREPARATION OF A SPINAL ANIMAL*

By Hugh McGuigan, M.D., and W. J. R. Heinekamp, B.S.,
Chicago, Ill.

IN the preparation of spinal animals to study the function of the central nervous system and to analyze drug action on this system various complicated operative procedures have been advanced.

In Sherrington's spinal animal the head is removed. Jackson (Experimental Pharmacology, 1917, p. 195 et seq.) after a major operation injects chloroform into the vertebral artery and in this way destroys the brain. The chloroform is prevented from returning to the heart by compression of the return venous circulation. This method is not always successful, and the heart is frequently injured by the chloroform. Luckhardt (quoted by Jackson) has succeeded in destroying the brain by injections of chloroform into the carotid ar-

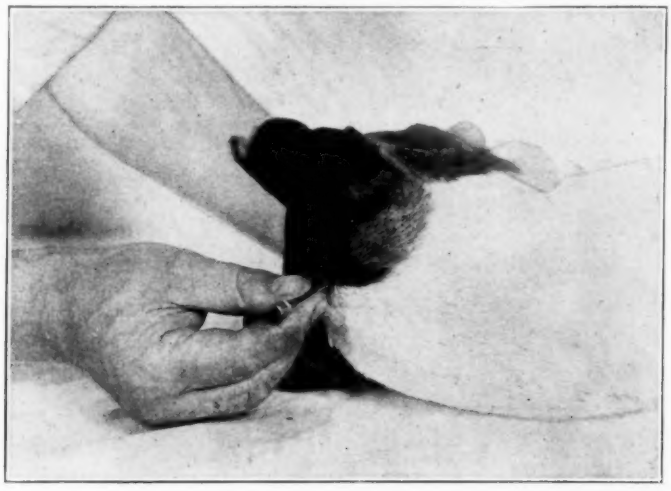

Fig. 1

tery. This method is somewhat less involved than injection into the vertebral artery, but has many of its disadvantages. Other workers have destroyed the brain by injecting a 3 per cent suspension of starch granules. In all these methods the blood pressure in the spinal dog, according to Jackson, is about one inch above the base line. From our point of view these methods are now of historical interest only, and show the usual steps in research—that is—from complicated to simpler and better methods.

*From the Laboratory of Pharmacology, University of Illinois, College of Medicine.

In the investigation of strychnine action by one of us (McGuigan, et al.: Journal of Pharmacology and Experimental Therapeutics, ii, p. 319; v, p. 469, and viii, p. 43) a similar advance from the complicated to the simple is recorded. In these latter investigations we finally injected drugs directly into the fourth ventricle, and into the spinal canal in other regions. In the preparation of spinal animals this method may also be used. One or two c.c. of chloroform (other drugs may be used) injected into the fourth ventricle is all that is necessary. The animal prepared in this way is far superior for work than one by the older methods of preparation.

METHOD

Anesthetize the animal and insert a tracheal cannula for artificial respiration. If in the experiment blood pressure tracings are desired these may be taken care of in the usual way. Then when the spinal condition is desired, bend the animal's head sharply on its chest and insert a medium-sized hypodermic needle between the occiput and atlas on the median line and press it into the ventricle (Fig. 1). There may be some slight difficulty in getting through, since in some animals there is an overlapping of the bones. However, if one keeps in the midline, the difficulty is very slight and once a puncture has been made a repetition is very easy. The needle usually drops through the resistance in the last step and an abundance of clear fluid is a striking indicator of the location. Frequently one strikes the respiratory center; with a little practice this can be avoided if desired. In the preparation of the spinal animal injury of the respiratory center is of no special moment.

ADVANTAGES OF THE METHOD

It is simple, bloodless, efficient, and has practically no effect on the blood pressure. Absorption from the ventricle is apparently slight, so that there is no direct action on other organs.

SEDIMENTING SUSPENSION OF LIVE BACTERIA ON A LARGE SCALE*

E. M. Houghton, M.D., and N. S. Ferry, M.D., Detroit, Mich.

IN the sedimentation of bacterial suspensions or broth cultures for the preparation of bacterial vaccines, or for the purpose of clarifying the broth before filtration in the process of obtaining toxins, where the question of time as well as quantity must be considered, laboratories have been compelled to resort to the use of a centrifugal machine run on the principle of a milk separator, such as the Sharples machine, which will permit of a continuous flow of liquid to and from the machine.

It has been found, however, that when the bacteria are being sedimented in a live state, it is rather an unsafe procedure for the operator unless some pro-

*From the Research Department, Parke, Davis & Company, Detroit, Mich.

tection is afforded against the fine spray, containing bacteria, which is given off from the liquid as it leaves the rapidly revolving bowl.

It has also been observed that the chances of obtaining a sediment or a filtrate in an uncontaminated state are rather doubtful unless the entire mechanism can be thoroughly sterilized before and after operation.

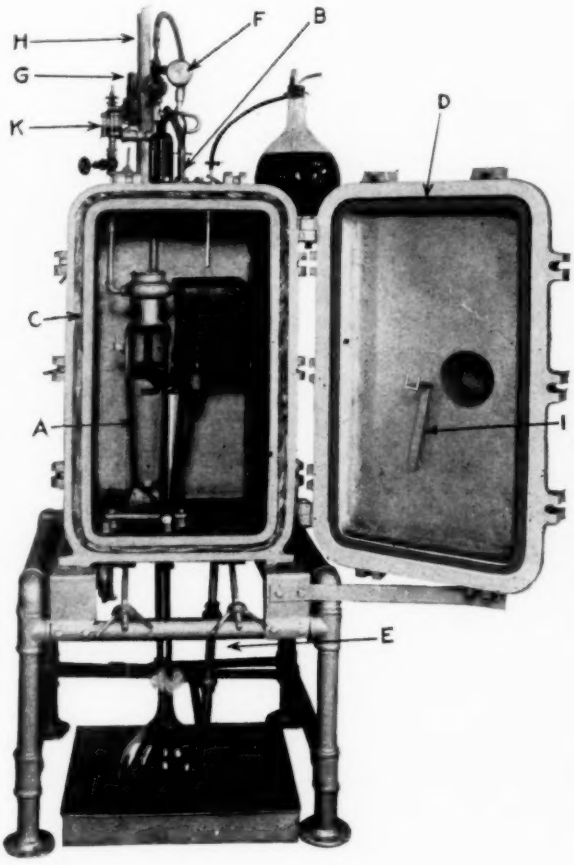

Fig. 1

A. Centrifuge.
B. Atomizer.
C. Cotton gasket
D. Rubber gasket.
E. Pipe to vacuum system.
F. Air pressure gauge.
G. Air safety valve.
H. Discharge pipe to centrifuge.
I. Handle to supply can.
K. Oiler to centrifuge.

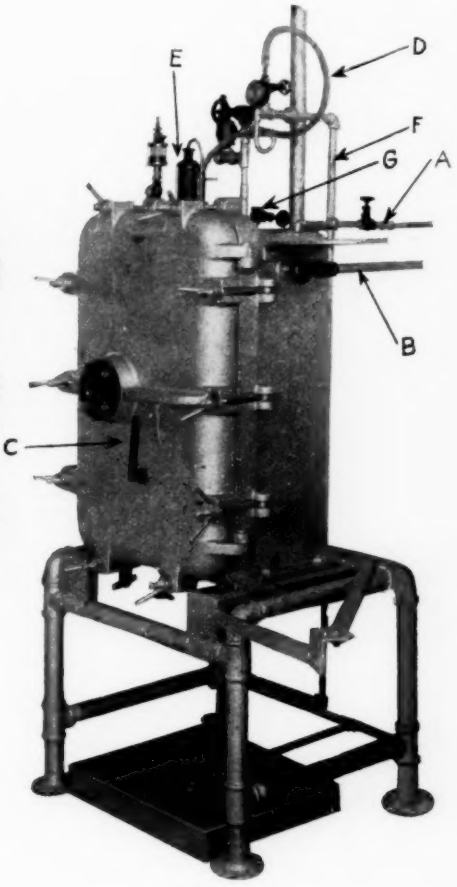

Fig. 2

A. Pipe to steam gauge.
B. Steam pipe.
C. Handle to supply can.
D. Air pipe to atomizer.
E. Bottle of germicide for atomizer.
F. Compressed air pipe.
G. Valve for siphon intake.

In order to obtain conditions as safe as possible for those in close proximity to the machine, and maintain, at the same time, an aseptic operation throughout, an apparatus has been devised according to plans suggested by one of us (E.M. H.) which fulfills the necessary requirements without influencing in any way the efficiency of the separator.

The apparatus in question consists of a cast iron jacket, opening on the

front, with a swing door, which completely encloses a Sharples turbine-driven laboratory centrifuge, including its supply can. The jacket is so constructed that it becomes an autoclave, when the door is securely shut, and the valves of the various pipes leading to the jacket are closed, in which the entire mechanism of the centrifuge can be sterilized with live steam at a temperature of 120°C. for any length of time deemed necessary. At the same time connection is maintained between the jacket and a vacuum system in order to facilitate the drying of the several parts of the machine, after the steam has been exhausted, without opening the door of the jacket.

To further insure the safety of the operator, in addition to a rubber gasket, on the inner surface of the door where it comes in contact with the rim of the jacket, is found a roll of cotton, soaked in a germicide, packed in a groove surrounding the frame of the door, making the door crack entirely germ-proof.

The apparatus is also equipped with a safety valve for the compressed air system as well as an automatic steam pressure gauge to doubly safeguard both the operator and the machine.

If it is found necessary to gain access to the machine any time before the parts can be autoclaved, sterilization of all exposed surfaces may be accomplished by means of a large atomizer, connected with the compressed air pipe and a bottle of some strong germicide, which is placed in the top of the jacket. This atomizer is so constructed that it will revolve at an angle of 360° in order to reach all sides and corners, and of such dimensions that it is capable of discharging with an air pressure from 30-50 pounds, causing the entire chamber to be filled with a fine cloud or spray and rendering any exposed parts perfectly safe to handle within a short space of time.

In order to control the flow of liquid from the supply can to the bowl, when the door is closed, a lever, having a handle on the outside of the door is made to connect with the faucet of the supply can so that it can be manipulated at will without exposing the inside of the jacket.

The apparatus has been given a thorough trial for several months on various vaccines and toxins, and has been found perfectly efficient as to its qualifications as a sterilizer, as well as a separator.

In centrifugalizing a certain lot of material the procedure is a follows: set up the machine for operation, clamp the door, shut all necessary valves, autoclave and then dry with vacuum. Start machine, allow suspension to siphon from flask, on top of jacket, into supply can. From there it will flow into the bowl and thence out of the nozzle through the funnel into the plugged flask under the jacket. The sediment will be found in the bowl and the clear filtrate in the flask, both uncontaminated.

AN APPARATUS FOR THE QUANTITATIVE DETERMINATION OF UROBILIN AND UROBILINOGEN*

By J. D. Boyd, B.Sc., Iowa City, Iowa

THE apparatus herewith described has been found convenient in making quantitative determinations of urobilin and urobilinogen. It has been in use for nearly a year.

It was constructed from a Hellige colorimeter and a hand spectroscope, and consists essentially of a hollow glass wedge which can be moved vertically before a fixed spectroscope. If the Hellige colorimeter is not obtainable, a similar apparatus can be made without much trouble.

The wedge is made by cutting pieces of clear glass to the desired size, and then grinding the edges with carborundum powder and water on a sheet of plate glass until the surfaces to be united approximate closely at the desired angle. (See diagram for dimensions.) The pieces are cemented together with Canada balsam; after the cement is partly set, the cell should be baked at approximately

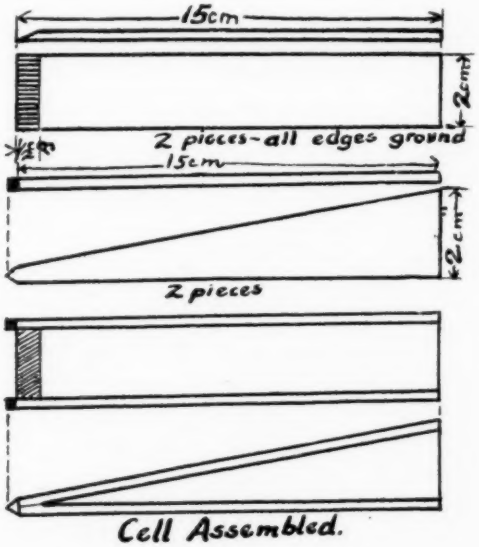

Fig. 1

120° C. for two or three days. To prevent the cement from being dissolved out, a little melted paraffin should be run down the seams, but should not be allowed to come in contact with the anterior or posterior surfaces of the wedge.

For those unfamiliar with the Hellige colorimeter the following short description may suffice.

The cell is supported on the distal panel of the colorimeter, which is provided with a pane of milk glass somewhat larger than the cell. This panel is movable up or down by means of a rachet, and is provided with a scale of the same length

*From the Chemical Laboratory of the Department of Internal Medicine, State University of Iowa, Iowa City.

as the depth of the cell, and graduated in hundredths. The spectroscope is attached to the fixed panel parallel to this by means of a U-shaped brass block provided with lugs.

The whole device is mounted against a board provided with a one-inch hole,

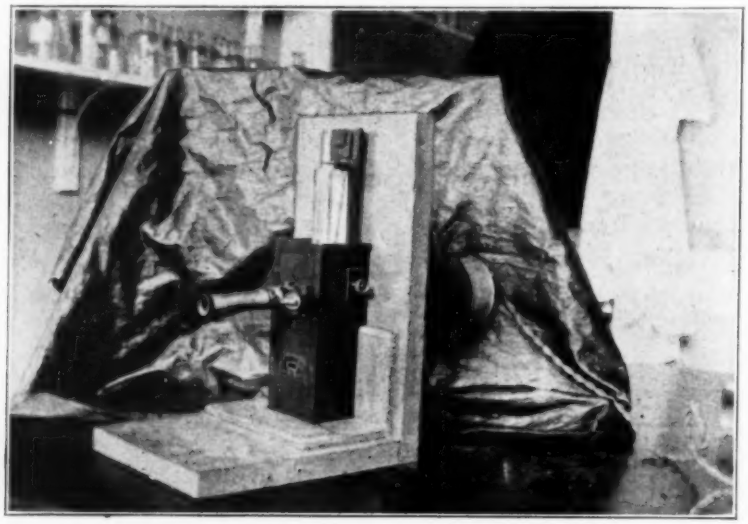

Fig. 2

Fig. 3

placed opposite the spectroscope, through which enters the light from a 40-watt electric lamp fixed to the back of the board. The lamp is enclosed in a tin cylinder. The apparatus is best used in a dark room.

PROCEDURE

The sample is prepared for examination according to the method of Wilbur and Addis. The cell which holds about 10 c.c. is filled with the solution, and the

point is found where the spectrum just disappears with moderate light, but reappears when the light is diminished by changing the light screen of the spectroscope. We prefer to examine for urobilin before adding the Ehrlich's reagent, but after acidification. The band is more sharp under these conditions. The cell used here is 1 cm. broad at the part corresponding to 100 on the scale.

CALCULATIONS

If the scale-reading be represented by R, then $\frac{100}{R}$ represents the number of times the sample can be diluted and the spectrum be just visible with the scale at 100. This value, multiplied by the previous dilution will give the total dilution value.

A SIMPLIFIED TECHNIC OF APPLYING THE ELECTRODES IN ELECTROCARDIOGRAPHY*

By David Felberbaum, M.D., New York City

THE usual method of applying the German silver plate electrodes upon the limbs of the subject in taking electrocardiographic records is more or less time consuming and untidy. This procedure is carried out by wrapping flannel bandages that have been soaked in warm saline solution about the limbs, enclosing the electrodes. These bandages soon become soiled and the drippings rapidly cover the surroundings of the patient. We have frequently found that when a number of consecutive electrocardiographic examinations are made, static interferences become very annoying, due to the crustations of salt, making conductors out of the chairs, etc.

To overcome these drawbacks I developed the following simple technic.

Fig. 1.—This illustrates the bag with the single layer turned back, showing how the bag is constructed.

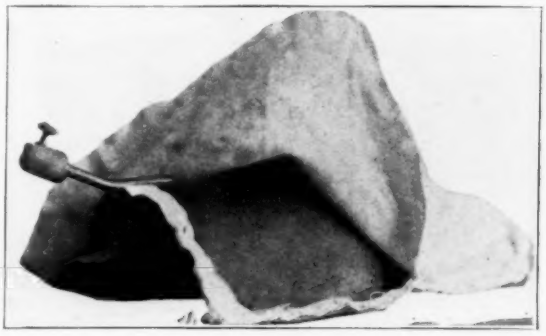

Fig. 2.—This illustrates the bag with the electrode placed between the two layers.

*Cardiological Department Montefiore Home and Hospital, N. Y.

A sort of bag, or better, mittenlike sack is made of heavy double-nap flannel. This is cut to correspond with the shape of the electrodes, but considerably larger. Four layers are sewed together to form the front, while a single layer forms the back of the sack. The single layer is sewed along the edge to the four layers for about two-thirds of its circumference (Fig. 1). The electrode is placed between the two after the bag has been thoroughly soaked in hot saline solution. The whole arrangement is then firmly bandaged down upon the limb of the subject by means of a wide rubber bandage. These bandages are about five inches wide and about 36 inches long, and are cut from the heaviest bandage gum supplied by the Hodgman Rubber Co., New York. The rubber bandage, besides holding this apparatus firmly to the limb, acts as an insulator, prevents the dripping, and keeps the bag warm. The rubber bandage is prevented from unrolling by placing an ordinary heavy rubber band around the end.

This arrangement is rapidly applied. Many sets of bags can be made so that each patient may be supplied with a clean one. They are neat, clean, portable, occupy very little space, and may be washed or even sterilized.

It has been repeatedly demonstrated that this arrangement causes less resistance in the string circuit than the former method. The resistance varies from a few hundred to two or three thousand ohms. I seldom need to employ the ten millivolt switch, and in that way always work with a highly sensitive string.

In conclusion, this method affords us a simple, rapid, portable, clean, and accurate means of attaching the electrode. The electrodes are kept free from corrosions and the resistance of the string circuit is kept at a minimum.

A SIMPLE METHOD FOR DETERMINING THE CAPACITY OF "TO CONTAIN" PIPETTES*

By Mary W. Wheeler, B.S., Albany, N. Y.

THE inability to procure accurately standardized "to contain" pipettes recently, made it necessary to grind down the slightly broken tips of some that had been in use, and then to restandardize these. Since it is necessary to determine the total volume of liquid in a "to contain" pipette and not the volume delivered from it, the usual method given in text books for standardizing "to deliver" pipettes is not applicable. However, this method requires but few modifications. The details of the method as modified are as follows:

1. A ground-glass-stoppered bottle filled with distilled water and a small covered dish (an ordinary stender dish) containing a piece of filter paper are weighed together on accurate analytical balances.

2. By means of a suction apparatus as shown in the accompanying diagram, water is drawn into the pipette from the bottle just to the graduation mark. Any water adhering to the outside of the pipette is then wiped off with the weighed

*From the Division of Laboratories and Research, of the New York State Department of Health, Albany, New York.

filter paper, which is then immediately returned to the dish and covered to prevent evaporation of moisture.

3. The bottle and dish are reweighed and the weight of the water contained in the pipette determined by difference.

4. The temperature of the water is determined just before or after filling the pipette. If the temperature of the room is practically constant, this is most easily done by finding the temperature of water in a breaker or bottle (similar to the one in use) standing near the apparatus and subjected to the same condition.

5. Five determinations are made for each pipette, the pipette being thoroughly dried between each determination by rinsing several times with alcohol and finally with ether.

6. From Tables 35 - 47 "Standard Density and Volumetric Tables," U. S. Bureau of Standards, Circular No. 19, correction for variation in temperature is made, the volume of the pipette being corrected to 20° C.

To check the accuracy of this method, the capacity of six German certified 2 c.c. "to contain" pipettes was determined.

The determinations made on one of these pipettes is given below in detail.

Pipette No. 2720. Two c.c. "to contain," certified as +.001 c.c. Temperature of Standardization 20° C.

(a) Weight of bottle of water, filter paper, and stender dish
(b) Weight of bottle of residual water and stender dish with filter paper
(c) Weight of water contained in pipette as determined by difference

(1)		(4)	
(a)	95.6485 gm.	(a)	93.1110 gm.
(b)	93.6526 "	(b)	91.1149 "
(c)	1.9959 "	(c)	1.9961 "

(2)		(5)	
(a)	91.7726 gm.	(a)	91.1149 gm.
(b)	89.7772 "	(b)	89.1195 "
(c)	1.9954 "	(c)	1.9954 "

(3)	
(a)	95.1068 gm.
(b)	93.1110 "
(c)	1.9958 "

Average weight of water contained in pipette, 1.99572 gm.

Temperature correction from Table No. 36, U. S. Bureau Standards, Circular No. 19.
Amount to be added to weight of water in grams as determined to obtain actual capacity of pipette in cubic centimeters at 20° C. = .00529.

1.99572 gm. weight of water in pipette
.00529 correction

2.00101 c.c. actual capacity at 20° C.
2.00000

+.00101 c.c. capacity error

The following table gives the results of the determinations of the six pipettes.

CAPACITY ERROR OF 2 C.C. "TO CONTAIN" PIPETTES

NO. OF PIPETTE	CAPACITY ERROR AS CERTIFIED	CAPACITY ERROR BY ABOVE METHOD*
2710	— .002 c.c.	— .00215 c.c.
2712	— .003 c.c.	— .00331 c.c.
2717	+ .002 c.c.	+ .00224 c.c.
2720	+ .001 c.c.	+ .00101 c.c.
2726	+ .002 c.c.	+ .00228 c.c.
2729	+ .003 c.c.	+ .00312 c.c.

In order to determine the error which would be introduced by not wiping off any water adhering to the outside of the tip of the pipette, the capacity of pipette No. 2720 was again determined. The method was the same as before

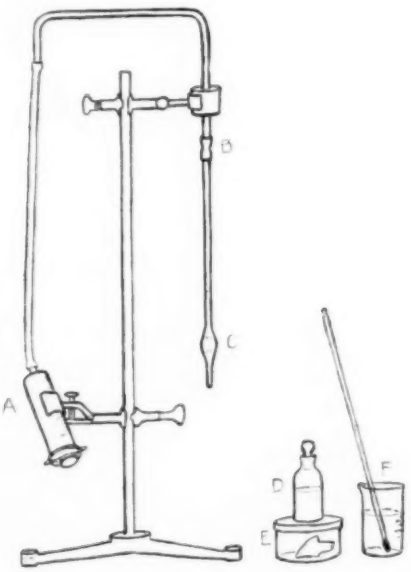

Fig. 1.—Apparatus for standardizing "to contain" pipettes. *A*, 5 c.c. syringe draw; *B*, rubber connection for holding pipette; *C*, "to contain" pipette to be standardized; *D*, ground-glass stoppered bottle containing water; *E*, stender dish containing filter paper; *F*, beaker of water containing thermometer, for temperature control.

except that the tip was not wiped with the filter paper. Only three determinations were made this time as the error was so apparent. The result was as follows:

Pipette No. 2720. Two c.c. "to contain," certified as +.001 c.c. Temperature of Standardization 20° C.

(a) Weight of bottle of water
(b) Weight of bottle of residual water
(c) Weight of water contained in pipette as determined by difference

(1)	(3)
(a) 36.7190 gm.	(a) 32.7226 gm.
(b) 34.7221 "	(b) 30.7261 "
(c) +1.9969 "	(c) 1.9965 "

(2)	
(a) 34.7221 gm.	
(b) 32.7226 "	Average weight of water contained in pipette, 1.99763 gm.
(c) 1.9995 "	

*The pipettes are certified to the third decimal place only. The last two figures in this column are added to show that a slight variation here would not alter the final result of the determination.

Temperature correction from Table No. 36, U. S. Bureau of Standards, Circular No. 19.
Amount to be added to weight of water in grams as determined to obtain actual capacity of pipette in cubic centimeters at 20° C.=.00564.
C.=.00564.

1.99763 gm. weight of water in pipette
.00564 correction

2.00327 c.c. actual capacity at 20° C.
2.00000

+.00327 c.c. capacity error

CONCLUSIONS

The method as given above for determining the capacity of "to contain" pipettes is simple, practical, and sufficiently accurate for laboratory use.

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ON THE DETECTION OF CHLORETONE IN MOTHER'S MILK*

By J. E. Blanner, Detroit, Michigan

IT IS a widely recognized fact that milk from lactating mothers may possess a foreign taste, odor or color following the ingestion of certain substances. As concrete examples, alcohol has been found,[1] likewise opium and morphine, zinc, iron, lead, arsenic, antimony, bismuth and mercury. These facts become of utmost importance in reference to the administration to the mother of such drugs as may be injurious to the child.

The extensive use of chloretone therapeutically calls for further research in this particular on this important drug. The presence of chloretone in the tissues, organs and fluids of the body after ingestion, has been conclusively demonstrated by Aldrich.[2]

The purpose of these experiments has been to determine the presence and amount, if any, of chloretone in the milk of lactating mothers. Humans and dogs were used as experimental subjects.

The method of demonstrating and estimating the presence and quantity of the drug was precisely that originated by Aldrich.[3] The efficacy of this method depends upon the characteristic crystalline form of chloretone, volatility with steam, and low solubility in water. A brief resume of the method may not be out of place.

The material under investigation, properly comminuted or digested if necessary, is subjected to steam distillation. Great care should be exercised in keep-

*From the Research Laboratories of Parke, Davis & Company.
My thanks are due to Sister Olimpia and Miss Peltier of the Providence Hospital, Detroit, who so kindly cooperated with me in the matter of securing patients and rendering other valued assistance.

ing all connections absolutely tight. The distillate is placed in a flask, which is connected with an upright condenser having a circulation of very cold water, and gently heated. If the test is positive, crystals of chloretone, long and feathery, will appear in the vicinity of the steam crest. A hand glass facilitates the detection in case of very small quantities. This test possesses much delicacy, as little as 1 mg. or 1/66 gr. having been readily detected.

EXPERIMENTAL

CASE I.—Mrs. J. Ten gr. of chloretone were administered and after one hour 60 mils of milk were taken. Results negative.

CASE II.—Mrs. A. One hour after the administration of 15 gr. of drug, 90 mils of milk were taken. Results negative.

CASE III.—Mrs. S. One hour after the administration of twenty gr. of drug 60 mils of milk were obtained. Results negative.

CASE IV.—Mrs. E. Two hours after administration of 10 gr. of chloretone, 60 mils of milk were taken. Results negative.

CASE V.—Mrs. McM. Two hours after administration of 15 gr. of drug, 75 mils of milk were obtained. Negative results.

CASE VI.—Mrs. H. Two hours after administration of 20 gr. of drug, 50 mils of milk were taken. Negative results.

CASE VII.—Mrs. B. Ten gr. of chloretone administered and 60 mils of milk taken three hours later. Results negative. Four hours from time of administration of drug, 30 mils were obtained. Negative results. Five hours later 40 mils. Negative results.

CASE VIII.—Mrs. C. Twenty gr. chloretone administered and samples averaging 40 mils taken at the end of every hour until five were obtained. Results proved negative.

CASE IX.—Mrs. D. Ten gr. of chloretone administered and one hour later 70 mils of milk obtained. Two hours from time of first administration 10 gr. more were given and one hour later 50 mils milk obtained. Two hours from time of second administration 10 gr. more were administered. One hour later 45 mils milk obtained. Two hours from third administration 10 gr. more were administered and 40 mils milk obtained. A total of 40 gr. chloretone had been administered in a space of eight hours. No positive test obtained.

CASE X.—Mrs. De T. Exact duplicate of Case IX. Negative results.

CASE XI.—Mrs. R. Fifteen gr. chloretone administered and one hour later 65 mils of milk removed. Two hours from time of first administration 15 gr. more were administered and one hour later 50 mils milk obtained. Two hours later 15 gr. more drug given and one hour later 40 mils milk obtained. A total of 45 gr. of drug given in a space of six hours all produced negative results.

The above mothers were normal women in every respect and were nursing their own infants throughout the period of experimentation. No effect on the infants was discernible; however, this would be very difficult as a normal infant sleeps the greater part of the day.

The following experiments were then performed on lactating dogs.

CASE A.—Lactating dog weighing 10.5 kilos was obtained seven weeks after parturition. The young were taken away at beginning of experiment. Dog normal in every respect except very thin.

Three grams of chloretone were dissolved in 3 mils of 95 per cent alcohol and poured into 60 mils of tepid water.

This suspension was administered per mouth to dog fifteen minutes after complete removal of milk by young. Dog immediately passed into profound sleep and remained in such condition for four days. At no time before recovery or after could any milk be obtained.

These results pointed to the necessity of a change in method of administration of drug.

CASE B.—Lactating dog, 10.5 kilos in weight, five weeks after parturition was taken from her young and milk completely removed by mechanical suction 15 minutes before ad-

ministration of chloretone. The drug 0.5 gm. was dissolved in the least possible amount of alcohol and intimately mixed with a portion of chopped meat. Seven hours later 15 mils of milk were removed and .8 gm. of the drug were administered in precisely the same manner as before.

This portion of milk to be known as Sample 1 gave negative results.

Seventeen hours later 85 mils of milk were taken and .8 gm. of drug again given. Sample 2 also gave negative results.

Twenty-four hours later milk removed from dog as completely as possible. Amount obtained 65 mils. Dog rather drowsy at this time. One gm. of drug administered. Sample 3 tested very positive. Estimated about 2 mg.

Seven hours later milk again taken from dog. Amount obtained 15 mils. At this time only .6 gm. of chloretone given as dog had become very drowsy.

Sample 4 gave positive test.

The following morning, seventeen hours later 30 mils of milk were obtained and 1 gm. of drug again administered. Positive test for Sample 5.

Seven hours later attempt was made to obtain more milk, but only about 2 mils were obtained. Administration of chloretone omitted this time. Stimulation, only, kept dog awake. Except for great sleepiness dog is normal.

The following morning milk was again removed. Seven mils were obtained. Chloretone 1 gm. again administered.

Sample 5, while positive, but barely perceptible, undoubtedly due to small amount of milk.

No drug was given in afternoon, neither was it possible to obtain any milk.

Seventeen hours later no milk could be obtained. Necessarily all experimentation came to an end.

The question here arises as to the effect of chloretone as an antigalactagogue. The results of the experiments on dogs point to such an effect, and this is in accordance with other findings in regard to chloretone as an inhibitor of the formation of bodily fluids. No such effect, however, was noticed in the case of human subjects. This undoubtedly is due to the small amount of the drug used, as weight for weight, the dog received *in toto*, twelve times as much chloretone as any human subject.

CONCLUSIONS

Chloretone is found in the milk only upon continuous administration of very large doses.

Upon the administration of 5 to 20 gr., the usual therapeutic dose, no trace is found even though administered several times in succession.

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The Journal of Laboratory and Clinical Medicine

VOL. IV. MAY, 1919 No. 8

Editor-in-Chief: VICTOR C. VAUGHAN, M.D.
Ann Arbor, Mich.

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Entered at the Post Office at St. Louis, Mo., as Second-Class Matter

EDITORIALS

The Michigan State Board of Health

MASSACHUSETTS was the first state in the Union to organize a State Board of Health. This was done in 1870 and the same year the State Medical Society of Michigan advocated the formation of a board in this state and a bill providing for such a board was introduced into the legislature of 1871. However, it failed to pass in that year, but was presented again at the next legislature in 1873 and passed. The legislature provided for a board of six men, eminent and interested in sanitary science, to be appointed by the Governor. The board was authorized to employ a secretary and determine his salary and the length of the service. In July, 1873, the board was organized and began to function. The secretary chosen was Dr. Henry B. Baker, who had had three years of service in the Civil War and appreciated the importance of the work which the board was to undertake. The first president of the board was Professor Robert Kedzie of the Michigan Agricultural College.

At that time the almost universal method of illumination in homes, in hotels,

in factories, in all but the larger cities, in all villages and country places, was the kerosene lamp. The tallow dip had passed away, and the general use of illuminating gas had not come in. The electric light was awaiting the developing genius of Edison, who about that time was a newsboy on the train between Detroit and Port Huron. Even in the homes of the wealthy where gas was in use, in kitchen or garret the unsafe oil lamp was still to be found. The daily newspapers carried almost constantly the headline "Another Kerosene Horror," with sickening details of some poor woman, possibly with her children, roasted like a martyr at the stake, set on fire by a lamp explosion. Cheap and inflammable benzine was sold as an illuminant under catch names such as "sunlight oil," "French burning oil," etc., with preposterous recipes to make the material nonexplosive. Packages of common salt colored with aniline were sold and guaranteed to "kill the gas." This special source of danger confronted the Michigan State Board of Health at the threshold of its duties. The oil was improperly refined, too much of the volatile matter retained in the kerosene, and no certain method of inspection was in use, the testing of the oil being too largely left to the seller. The result of the investigations of the board led to the adoption of the "Michigan oil tester," with closed cup inspection and the flashing point as line of danger. These were made the legal methods of testing and a state oil inspector was appointed to have charge of this business. After this provision, the people of the state found a safe light. The fight, however, between the venders of oil and the people went on for nearly twenty years. It was fought with great bitterness and frequent changes in the law were adopted by the legislature.

On account of the large lakes which mark its boundaries and the many beautiful inland waters, Michigan had even at that time come to be known far and wide as a desirable summer resort. The inviting cool waters tempted the old and the young, and cases of drowning were common. Drs. Kedzie and Baker, after months of experimental investigation, developed a scientific method of resuscitating the apparently drowned. This method, long known as the "Michigan method," illustrated on posters was to be found at bathing places on the shores of all our lakes, both great and small. A few years ago a distinguished English professor of physiology demonstrated in one of the university buildings at Ann Arbor what he called a new and scientific method of treating the apparently drowned. After his lecture and demonstration, he was shown the description and cuts adopted by Michigan nearly forty years before. He read the description carefully, scrutinized the illustrations, and freely affirmed that in no marked particular was his method an improvement upon the Michigan method. The posters and leaflets with illustrations of this method can be found in the annual report of the Michigan State Board of Health of the year 1874. Thousands of these leaflets have been distributed over the state, they have been several times revised, and the latest edition which deals with the treatment of the electrically shocked as well as the drowned, may be found in the report for 1897.

It is interesting to note that as early as 1878 Dr. Henry Lyster, of Detroit, and the Honorable Leroy Parker, then of Pontiac, now living in Washington, D. C., offered a plan for the examination of candidates in sanitary science. The board had in mind the improvement of the health service of the state, thinking

that calling attention to the fact that the board would examine candidates would tend to have local boards of health appoint health officers who had thus demonstrated their suitability. Again the State Board of Health of Michigan was ahead of the movement now evidenced in our universities by the creation of courses leading to the degree of Doctor of Public Health by more than forty years. It was the intention of the board that only such persons as had passed this examination would be eligible to the position of health officer. The first examination was conducted by the board, July 14, 1880, and there were two successful candidates. The reason this procedure was so short-lived was that of the lack of applicants and the failure of the public to appreciate the value of the expert. Even up to today, any village doctor who has practiced medicine for five years without demonstrating any knowledge of the prevention of disease is eligible to the highest office in sanitation within the gift of the state.

In the seventies it was common to find the walls of the houses, even of our most prominent and prosperous citizens, covered with highly colored wall paper. Dr. Kedzie studied this paper and found that it was loaded with arsenical colors. He prepared a report in a separate volume with samples of the poisonous wall papers and distributed it in November, 1874. The title of this volume was "Shadows from the Walls of Death." The book contained a hundred or more actual samples of wall paper which had been tested and proved to contain arsenic. This raised a great cry from the manufacturers of these papers and the matter finally reached hearings before a committee of Congress. However, the people were in the end victorious and no arsenical wall papers have been found on the market for many years. Slow arsenical poisoning resulted from the use of this paper. The paste by which the paper was attached to the walls contained microorganisms which, finding abundant nourishment in the paste, grew, multiplied, formed hydrogen gas, which combined with the arsenic in the paper and was diffused through the room in the most deadly form of arsenic known to science. It may be interesting to note that in the world's great war the Germans attempted to use this gas in their barbarous methods of combat with the allies.

Up to the time of the creation of the board, little or no attention was paid to the construction, warming, and ventilation of schoolhouses. In its first report (1873), a paper on this subject was presented by Dr. Kedzie. This led finally to the passage of the law compelling the submission to the board of health of the plans for heating and ventilating of state buildings.

Meteorologic observations were first begun in Michigan in 1834, but the observations were irregular, sporadic, and inefficient. In 1864, Dr. Kedzie at the Agricultural College began the systematic study of meteorologic conditions. The State Board of Health took this up and from 1870 until the establishment of the Meteorologic Service by the United States government this work was continued in Michigan. It will be seen from this that the study of meteorologic conditions was begun on a systematic plan by the State Board of Health and was probably the first continued effort ever made to forecast the weather.

In the seventies of the last century there were no trustworthy vital statistics. We had no official and satisfactory figures showing either the birth or the death rate. Both were matters of guess. Michigan rapidly developed its mortality

statistics and is now known as one of the group of "original registration" states upon which the United States government relies for its vital statistics.

There is even now in no city, in no state, any reliable set of statistics concerning the prevalence of sickness,—what is known as "morbidity statistics." At the meeting of the Michigan Board in July, 1876, Secretary Baker presented a method for compiling such statistics and was authorized to proceed with it. These statistics were collected as long as he remained secretary of the board, but later fell into desuetude. In each of the annual reports since 1876 up to the time Secretary Baker was dismissed from service there will be found a compilation of these statistics. By means of these figures Dr. Baker established curves which showed graphically that sickness from pneumonia is quantitatively related to atmospheric temperature; in other words, the colder the atmosphere, the more sickness from pneumonia.

The Michigan Legislature wisely left the question of what are the "dangerous communicable diseases" to the State Board of Health. It may be of interest to note the years in which various diseases were placed on this list. Measles, whooping cough, scarlet fever, typhoid fever, smallpox and cholera were listed in 1873; diphtheria in 1875; puerperal fever and erysipelas in 1878; typhus fever in 1879; German measles in 1886; croup and so-called typho-malarial fever in 1889; tuberculosis in 1893; yellow fever, glanders, rabies, tetanus, pneumonia, influenza and cerebrospinal meningitis in 1895. Venereal diseases did not go on the list until 1917.

The stringent law making it obligatory upon every and each householder, hotel keeper, keeper of a boarding house, or tenant and physician, to immediately give notice to the health officer of any communicable disease within their knowledge was passed in 1883. From the time of its organization, the board began to discuss methods of reaching the masses in giving information concerning the restriction of disease and the preservation of health. At the meeting of the board on April 9, 1878, President Kedzie recommended that sanitary conventions or meetings in various parts of the state be held to discuss subjects relating to sanitation. The first convention of this kind was held in Detroit, January 7 and 8, 1880. From that time, so long as Secretary Baker retained his position, such conventions were held at least twice a year in various parts of the state, and the low death rate and the prolonged life of which the state is now justly proud were largely due to this method of diffusing knowledge through the masses of the people.

Writing about these sanitary conventions in 1898, Dr. Lee of the Pennsylvania State Board of Health gives a laughable discussion of his first attempt to follow the Michigan plan. He called a sanitary convention in the city of Philadelphia, prepared a splendid program, and invited distinguished sanitarians from all over the United States to participate. When the day came, he and his invited guests occupied the stage, but the seats in front of them were empty. Dr. Lee says:

"To reduce the statement to a mathematical proposition, I would say the size of the audience at a state sanitary convention will be inversely as the square of the population of the place in which it is held."

This the Michigan State Board of Health found to be true in a general way.

In small places, the whole population turned out, while in the larger cities the attendance was small.

One of the early good works done by the Michigan State Board of Health was the investigation of those diseases in animals which are dangerous to man. Although the laws of Michigan as early as 1869 empowered the governor to appoint three commissioners, the law was inactive until the State Board of Health took up the matter. In the first law there was no appropriation with which the work could be done. In 1885, a law was passed authorizing the Governor to appoint three commissioners and a state veterinarian. In this way came into existence our highly efficient State Live Stock Sanitary Commission.

Michigan has the enviable reputation of having the lowest death rate among the states which have been in the registration area since 1900. This is largely due to the work of the Michigan State Board of Health. In the seventies, before Koch had discovered the specific cause of this disease, the State Board of Health began to teach the people of the state that tuberculosis is a transmissible and therefore a preventable disease. As has already been stated, tuberculosis was placed on the reportable list in 1893. In 1894, and at each successive legislature thereafter until it was finally accomplished, the Michigan State Board of Health urged the legislature to build a state tuberculosis sanatorium. Finally this was accomplished, and we have today not only a state sanatorium but all of our larger cities have their sanatoria and at least eight counties have provided such institutions.

It became evident to the board that while it was reaching the adults in the state, something must be done to reach the children. This led to a most beneficent law, passed by the legislature of 1895, and modified by that of 1897, which requires that there shall be taught in every public school in Michigan the modes by which the dangerous communicable diseases are spread and the best methods for their restriction and prevention. In order to make it possible to comply with this statutory requirement, the board issued and distributed a leaflet which in a short and concise manner states how the dangerous diseases are spread and how they may be restricted and prevented. The teachers in the public schools were slow to take up this duty. Most of them were incompetent, many were indifferent, and a few were positively hostile to the movement. Even now, however, it is coming to pass that every intelligent educated man and woman and child over ten years of age knows what diseases are transmissible and what procedures are necessary to prevent their spread. When asked by a Massachusetts man why tuberculosis is much less prevalent in Michigan than in his state, the Michigan man replies, "On account of the greater sanitary knowledge and intelligence of the people of the state of Michigan."

Some of the wise recommendations of the board have not yet been adopted. Among these we may mention the recommendation made in 1877 that the office of coroner be abolished and that experts be selected to make the physical examinations in cases of persons found dead or suddenly dying.

The board has constantly given intelligent attention to the question of water supply and systems of sewerage. It long recognized the fact that much money is foolishly spent, especially by small cities and villages, in providing these utili-

ties. Recently the board has been given legislative authority to pass upon the water supplies and sewage disposal of various municipalities in the state.

In the eighties, the cheese industry and other milk industries in the state were threatened with serious loss on account of the numerous cases of poisoning with cheese, ice cream, and other milk products. All kinds of theories were offered to explain these accidents. In 1884 the board took up this matter and showed that the poisons formed in milk products were due to bacterial contamination. Now cases of poisoning of this kind are so rare that some people deny that they ever occurred. These researches begun by the board in 1884, led to the suspicion that milk and milk products were accountable for the high infantile mortality. At that time, about 26 per cent of the children born in the state died before they reached one year of age. This was true not only in Michigan but all over the civilized world. The cause for this high infantile mortality was attributed by some to the nature of the soil on which the house was built, by some to the prevailing wind, while others attributed the high death rate to spots on the sun. It was finally shown that the high infantile mortality was due to poisonous milk, and the death rate has been reduced more than half.

In 1884, the board of health with the backing of the Michigan Business Men's Association asked the University of Michigan to build, equip, and man a state laboratory of hygiene. This was not accomplished or at least the building was not in readiness and in operation until 1888. Even with this delay, this was the second laboratory devoted to hygiene and sanitation established in the world, the first being that of the University of Munich which began operation in 1884. In this laboratory suspected food and drink were examined for health officers and for private citizens. Some things happened about that time which doubtless have been forgotten or were never known to the majority now living. The superintendent of a water company in a city in the northern peninsula sent a sample of water to the laboratory for examination. It was reported as unsafe, and the superintendent being financially interested, made no report to the people of this condition. They continued to use the water for about three weeks, during which time many hundred cases of typhoid fever developed in the place. Then the health officer sent a sample of water to the laboratory. He was surprised to receive a telegram that the water had been condemned three weeks previously. The people of the village went after the superintendent of the water works with a rope. Just what happened no one ever knew, but the superintendent has never been seen in that village since.

It is impossible to give any figures showing the number of lives that have been saved, or the financial saving that has resulted to the state from the labors of the Michigan State Board of Health. Whatever credit is due this board during the first thirty or more years of its existence is largely due to a man now living in comparative obscurity, Dr. Henry B. Baker, its efficient secretary during those years. So long as the board had the appointment of its own secretary, the only salaried officer on the board, politics did not touch it. But the time came when politicians became hungry for this salaried position. The legislature was induced to take the appointment of the secretary away from the board and place it in the hands of the governor. From that time on, and so long as it continues, politics has and will continue to seriously interfere with the work of the

board. And now there is a bill before the legislature abolishing the Michigan State Board of Health, making the secretary the sole executive officer, and putting everything in his hands. It should not be understood that there has been no efficient secretary since this change was made, but with every incoming governor the secretary must be changed and scientific carefully planned work can not be done. The bill now before the legislature provides that in place of the State Board of Health there shall be an Advisory Council of Health, but this council has no control over the secretary. If we are going to make the Michigan State Board of Health a political football, let us so declare publicly and have a health commissioner appointed by the governor, responsible only to the governor, and liable to replacement with every change in the gubernatorial office. There is no need of camouflage. Either the secretary should be the whole thing, or he should act under the direction of the board. An advisory council is camouflage; nothing more, nothing less. Crippled as it has been by having no control over its executive officer, the board has done, and is still doing, some most valuable work. The tuberculosis survey of the state, carried out in the years 1915 and 1916, was without doubt the best piece of work ever done in any state in this country or in any country in our fight against tuberculosis. The work which is now being done in combating the venereal diseases is important, and should be continued. A bill has been written, permitting the commissioner of health not only to be the sole administrator of health matters, but to appoint a health officer in every county in the state. This is so plainly political that it has probably died a natural death.

There is complaint made that so few young men are now willing to undertake public health work. The history of the Michigan State Board of Health, and especially that of its long-time and most efficient secretary, is not likely to induce bright and competent young men to undertake such work. As has been stated, the man who did so much for the public health of Michigan, who had labored so long in this field that he was quite unprepared to do anything else, like the faithful old horse, is turned out to live as best he may, and to die uncared for.

—*V. C. V.*

The Catalytic Power of Blood and Solid Tissues

THE remarkable series of papers by Burge* and his associates which have appeared during the past two years on the relation of enzymes, which have the power of releasing oxygen from hydrogen peroxide, to many of the physiologic functions of the body, have awakened considerable interest. These enzymes, which Kastle named "Catalases," have been found by Burge to be intimately associated with the oxidative activity of the body. In general he has found an increase in the catalase content of the blood and tissues of animals in which oxidation is large or has been increased, and a decrease in the normal amount in conditions where oxidation is decreased. He believes that variations in the activity of these enzymes explain one of the physiologic differences in used and

*Burge: Am. Jour. Physiol., see volumes xli to xlviii inclusive.

unused muscle; the difference in the ratio of heat production in large and small animals; loss of weight during starvation and during thyroid feeding; body changes during emotions and during anesthesia; shock; and the cause of the specific dynamic action of foods.

The function of catalase is not known. A number of theories have been advanced; one holds that it destroys peroxides which are formed during the life of the cell and which are harmful to the organism; another that it prevents excessive oxidation within the cell, and still another that it is the substance which releases oxygen from hemoglobin for use by the cell. The work of Burge appeared to indicate that catalase has an important role in oxidation.

Recently Becht† has published a convincing report of work in which he has been unable to reproduce Burge's results. Using what he believes to be accurate and superior methods and making a large number of duplicate analyses he has found a thousand per cent variation in the catalase content of blood of dogs kept under identical conditions, and wide variations in the blood of different species. He noted a decrease in the catalase content of the blood following thyroid feeding, which is exactly the opposite found by Burge; likewise an increase in place of Burge's decrease in the blood during anesthesia. He believes that it is impossible to accurately determine the catalase content of solid tissues by present methods. If Becht's criticism of Burge's work is correct, what appeared for a time to be a master key to a portion of physiology has failed to open the lock.

—*R. G. P.*

The Selective Service Act and Its Lessons

WHATEVER may be said about the functioning of other branches of the War Department, it must be admitted by all that the Provost Marshall General was fully equal to the heavy task assigned to him. He and his assistants deserve every honor that the government can bestow upon them. In April, 1917, when a state of war against Germany was proclaimed, we had a small regular army and the national guards of the different states which had recently been federalized. By June, 1917, these organizations had been augmented by volunteer enlistment to a combined strength of 465,985—altogether too small an army to put into this great war. Indeed it was not deemed wise to provide for an initial army, under training at least, of less than one million. How was such an army to be raised, quickly and with the least disturbance of agricultural and industrial affairs? During two years of the Civil War a half-way conscription was in effect, but it authorized the paying of bounties and the hiring of substitutes. It was resented quite generally throughout the northern states, and in New York it led to a temporary condition of anarchy. The practical result was that it contributed a forced service from only 46,347, out of a total draft of 776,829.

The Selective Service Act of 1917 was wisely enacted, promptly and justly executed, and it gave in the short space of little more than one year an army of more than three million, and had the war continued, this number might have been doubled in another year. The registration, selection, and mobilization

†Becht: Ibid., 1919, xlviii, 171.

moved through all phases with as little friction as could be expected of a newly invented, but scientifically devised machine. The behavior of the National Guard and the National Army on the battle fields of France has demonstrated not only the patriotism, but the fighting efficiency of our newly made and hastily trained soldiers. It is not too much to state that the war was fought and the necessary aid rendered our allies by civilian soldiers, for although seven divisions of so-called regulars participated in the fighting, more than two-thirds of these were recent recruits. These facts should justify inquiry as to whether or not we should choose between a large regular army in which being a soldier is a life work, and universal military training, which would do away with the profession of arms and make us ready at all times and on short notice to raise an efficient army of sufficient size to cope with any emergency that may arise in the future. The advice to disband the regular army and burn West Point, said to have been given by an officer returning from France, is worthy of consideration.

There were 4,557 local boards, an important member of each of which was a physician. For the most part, the doctors on these boards, as well as those on the district boards, did their duty in a commendable manner. It is true that there are stories told of men with glass eyes and cork legs being passed, but the Provost Marshal General makes the following statement in regard to these reports:

"Rumors here and there in the public press stated that the camp surgeons had discovered among the men accepted by the local boards some with glass eyes, some with cork legs, and some with other obvious disqualifications. If such men were found, it is no disparagement for the local board surgeons: for it is safe to assert that such grossly defective persons came from the contingent of about 20,000 men who had never appeared before the local boards, but had been gathered up by the adjutants-general and sent direct to the camps. There is no ground for supposing that the local board surgeons were either incompetent or careless to that extent. The spirit of their practice was to make all intendments in favor of the government; but nothing permits us to suppose that they held or did send to camp any men with cork legs or glass eyes."

It is not denied that the doctors on both the local and district boards made mistakes. They made some, and in the aggregate these grew into many. Nowhere else did the examining physicians fall down in practice more frequently or more sadly than in their failure to recognize tuberculosis. The high death rate in some of the camps from this disease during the first few months of service makes this point incontrovertible. Not only did the doctors on the local boards fail lamentably in this matter, but the experts on the special boards in the camps stumbled frequently and badly, and their mistakes were the more unexpected and the less excusable. It has long been a matter of common knowledge that the ordinary practitioner of medicine is grossly lacking in the skill necessary to detect incipient tuberculosis, but when the man posing as an expert in this disease accepts as soldiers men with the disease so far advanced that death results in less than six months, there is something wrong. Physicians as a rule when they become officers object to being assigned to the examination of

recruits, and doubtlessly many of them perform this function when assigned to them in a perfunctory way, but this is a serious mistake. There is no better opportunity for training in physical diagnosis. When a patient comes to a doctor in civil life, the patient usually partially at least, diagnoses his own case by calling attention to some organ where, in his opinion, his trouble resides. Too often the doctor follows this lead, and gives his undivided attention to the part in question, while the grossest lesions in other parts of the body may pass undetected. This is a fault which the wise physician will soon remedy; even now the more intelligent patients recognize it.

In the first draft, the number of registrants enrolled June 5, 1917, was 9,586,508. This means that, with the exception of the relatively few who were physically unable to report or who tried to evade the draft, there were that many men of draft age in the country.

The number of men actually physically examined in the draft by the boards was 2,510,706, of which 730,756 (29.11 per cent) were rejected. Of those accepted by the local boards and sent to the camps, 5.8 per cent, taking all the camps together, were rejected by the expert boards. During the Civil War, the percentage of rejections averaged about 26 per cent. The Provost Marshal makes the following statement on this point:

"In view of the great advance since that date in standards of medical diagnosis and physical perfection, the foregoing figures indicate a decided improvement in national physical condition during the past two generations."

So far as the study has been made, there is practically a tie in the percentage of rejections as between urbans and rurals. Attempts to deceive the medical examiners were made only to a slight and negligible extent. The report states:

"Here and there a local board reports a locality as showing 50 per cent of attempted falsifications, but these instances were sporadic and represent some local obliquity of morals."

In the report it appears that venereal diseases were accountable for only 4.27 per cent of the rejections, but this does not correctly indicate the prevalence of these diseases among the men because unless the man was rendered quite unfit or was a positive danger to others, these diseases fortunately did not warrant rejection. Had this been the case, the percentage of rejections from this cause would have been much higher. Statistics show that venereal disease is much more prevalent among civilians than among soldiers. It has been positively demonstrated that instead of civilian communities needing protection against soldiers so far as venereal diseases are concerned, the soldier needs protection from civilian communities. In the record as it stands, it appears that defects of the eye and of the teeth were most numerous. It is gratifying to note that alcoholism and the drug habit were infrequent. Mental deficiency and nervous disorders show up rather alarmingly.

The ratio of physically qualified to physically examined was less than 60 per cent in Maine, Rhode Island, Vermont and Pennsylvania; from 60 to 65

per cent in New Hampshire, West Virginia, and Massachusetts; from 65 to 70 per cent in New York, Kentucky, New Jersey, Louisiana, and Nevada; from 70 to 75 per cent in Maryland, Virginia, North Carolina, South Carolina, Georgia, Florida, Mississippi, Arkansas, Tennessee, Missouri, Illinois, Indiana, Ohio, Michigan, Wisconsin, Colorado, New Mexico, California, Oregon, Washington; from 75 to 80 per cent in Alabama, North Dakota, Nebraska, Kansas, Oklahoma, Texas, Arizona, Utah, Wyoming, Idaho and Montana; 80 per cent and over, in South Dakota. It is doubtful how much stress can be placed on these figures. As they stand, they indicate a physical inferiority in New England and Pennsylvania, even when compared with the Black Belt of the South, and this is more striking when the comparison is made with the plain and mountain states of the West. The Provost Marshal General says:

"The causes for rejection when ascertained will be of great sociological and medical value, but in the present emergency the time and labor to examine in detail two and one-half million records can not be spared."

Of the 3,082,949 called by the local boards, 252,294 (8.18 per cent) failed to appear for examination. Of these at least three classes were not "slackers": (1) Many enlisted after registration but failed to notify their local boards of their enlistment; (2) some died; (3) many were transferred to other boards but were not so reported. The numbers estimated as belonging to these classes are (1) 85,000; (2) 750; (3) 1500. This leaves about 150,000 to be accounted for. It is believed that 100,000 of these were aliens. Many, especially those living along the Canadian border, passed over the line, preferring to serve with their native armies. Other aliens were so ignorant that they did not understand. The real "slackers" are estimated at about 50,000, an average of about 10 for each local board.

The question is asked whether the physical requirements as set forth by the Surgeon General were too strict or not. The Provost Marshal General remarks:

"On this point the civilian surgeons have expressed varied opinions. A large majority say that the physical requirements are not too exacting, but a considerable number deem the physical requirements too strict in many respects, notably as to the weight and height relation, teeth, eyes and feet, and contend that the regulations as strictly applied tend to exclude many capable and efficient men.

"For example, one board cited a case of exclusion for flat-foot of a man who had for many consecutive seasons endured the hardships of a guide vocation in the Canadian forests, and the prevalence of flat-foot among the sturdy negroes in the South was frequently commented upon."

As to flat-foot as a disqualifying condition, even orthopedists are divided. But that, on the whole, the requirements were not too strict—indeed were not strict enough—is shown by the large numbers that subsequently had to be transferred to development battalions. Defects in teeth, eyes, and in many other particulars should have been remedied in civil life when these boys were in school. The nation that is not interested in the physical education of its children is not prepared for full and satisfactory achievement in either peace or war.

It will be of interest to inquire briefly into the claims for exemption. On this point the Provost Marshal General states:

"Of the total number called (3,082,949) 1,560,570 (50.62 per cent) made claims for exemption. Of the claims made 1,215,049, or 39 per cent of the persons called, or 77.86 per cent of the claims made, were granted. Of 1,419,678 claims made to local boards, 1,161,206 were granted; that is 81.79 per cent of claims made before local boards were granted; 140,892 claims were made to district boards and 53,843, or 38.21 per cent of claims made were granted. * * * Of the total claims granted (1,161,206) 859,150 or 73.99 per cent of all claims granted were on the ground of dependency, 228,452 or 19.67 per cent were on the ground of alienage, 67,716 or 5.83 per cent were on the ground of vocation, 3,887 or .34 per cent were on the ground of religious belief, and 2,001 or .17 per cent were on the ground of moral unfitness."

In considering these figures, it must be borne in mind that the national purpose was to assist our allies, not only with armed forces but industrially in the manufacture of munitions, guns, airplanes, ships, automobiles, etc., and with food. Therefore it was not only necessary to make soldiers, but to keep the wheels of industry going and at the same time to produce enough food to supply ourselves and our allies. We were compelled to provide for military, agricultural and industrial needs. Since the world began no nation has been wise enough to make an equal distribution of the burdens of war among these classes. War has always given opportunity for heroic sacrifice on the part of some, and selfish gain on the part of others. In the first flush of patriotism the doctor who for any reason was compelled to stay at home promised to divide his fees with the families of brother practitioners privileged to go. We may now ask ourselves to what extent this good intention has been realized. At first, the manufacturer of munitions stated that he would seek no large gains,— and so it ran through all occupations and callings. We may never know to what extent this altruistic spirit has dominated in actuality. However, man has not yet acquired the wisdom necessary to run the governmental machinery with equal justice to all, and with our many shortcomings the first real conscription attempted by this country has been fair in its application, prompt in its execution, and efficient in its results.

The Provost Marshal General's optimism concerning the physical improvement of the nation since the Civil War has questionable support in facts. Be this as it may, the following are some of the lessons which seem to be indicated by our experience with the draft:

(1) At least one-third of our young men are unfit physically for military service. If those who proved unfit after trial were added, this fraction would be much larger. This is the real test of any man's fitness for military service. The number of unfit, under any estimate, is too large and indicates lack of proper physical training, or the presence of unsanitary environment, or the inheritance of marked physical defects. Doubtless all of these are factors contributing to this delinquency. The causes should be ascertained and steps taken for their removal.

(2) We have among us too many low-grade aliens. So far, the records fail to show to what extent the alien stock among us has contributed to our physical

defects, but the facts given concerning the relative ratio of physically qualified to physically examined are suggestive at the least. If the average physical condition of the young men of Alabama with its large negro population is better than that of Pennsylvania with its large foreign white population, it is time that greater restrictions should be placed on immigration. The report does not give sufficient data on this point, and we await details concerning rejections for physical disqualifications.

(3) We certainly should take it to heart and recognize that, so far as the physical training of our youth is concerned, we are sadly at fault.

—*V. C. V.*